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JOURNAL.

TEXT-BOOK OF MEDICINE.

PRACTICE

OF

MEDICINE

BY EMINENT MEDICAL
SPECIALISTS AND AUTHORITIES

EDITED BY

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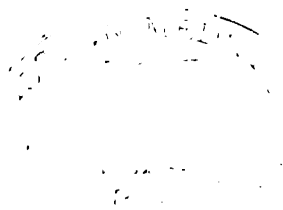
PREFACE.

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A CONSIDERABLE lapse of time has occurred since the publication in this country of a text-book similar to that now submitted to the public. The advances in every branch of medicine have during the interval been so great as to create a want for a work reflecting modern English teaching, and it has been felt that this can be most satisfactorily met by the united efforts of several writers who represent different important schools in the United Kingdom.

In arranging the scheme and determining the scope of the work, certain points have demanded consideration, and it has by no means been easy to arrive at a decision regarding them. The wisdom of including a preliminary discussion of general etiological and pathological problems, by way of introduction to the more practical portion of the work, has been carefully weighed, and the conclusion reached that such a section would be of real utility. The position of cutaneous diseases has also been a subject of anxious deliberation. Although fully recognising that in every medical school Dermatology ought to have the thorough teaching which can only be given by a specialist, it has seemed inexpedient to exclude diseases of the skin from a text-book on the Practice of Medicine. Another matter requires a word of remark. Certain symptoms, occasionally dignified by the title of separate diseases, will be sought in vain under individual headings, but will be found as parts of the subjects to which they properly belong.

It only remains for the Editor to return his grateful thanks to all his coadjutors for the unfailing consideration and loyal support which they have rendered in the production of these volumes, and to express the profound regret occasioned by the death, during the progress of the work, of Professor Kanthack, which has inflicted a grievous loss on scientific medicine

<div align="right">G. A. GIBSON.</div>

EDINBURGH, *April* 1901.

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INTRODUCTION.

THE GENERAL PATHOLOGY OF DISEASE.

WITHOUT a knowledge of the causation and the processes of disease, it is impossible to appreciate the nature and symptoms of a lesion. The physician, in making his diagnosis, should always reflect upon the changes, structural and functional, which might lead to the production of a symptom, or any complex of symptoms. A knowledge of pathology will lead him not to confound the symptom with the disease, either in diagnosis or in treatment. Every disease has a cause. It may be, and often is, easy to detect this cause, and to trace the relation between cause and effect, but obscure symptoms may be due to changes in the body, of which those unacquainted with pathology must necessarily remain unaware. Pathology enables the physician to determine the limits and mode of treatment, and also the probable or possible prognosis of a case, for it teaches the reactions of the body and its tissues, the understanding of which is as necessary to him as is a familiarity with Euclid's axioms in the study of mathematics.

A student working in the wards soon learns that without a thorough knowledge of pathology and pathological methods a sound diagnosis is often impossible; he finds that the post-mortem room is one of the best training schools for the physician, for there it is that he is brought face to face with the diagnosis he has made, that imagination is controlled by fact, and that what appeared to be mysterious and inexplicable finds its natural explanation. Before studying disease itself, it is necessary to consider generally but carefully the processes, causes, effects, and concomitants of disease.

THE REACTIONS OF THE BODY AND ITS TISSUES.

Degenerations, inflammation, and repair, hypertrophy and atrophy, are the most essential and elementary amongst the processes of disease. Of these, degenerations and atrophy may be said to be retrogressive reactions, through which the functional activity of an organ or a tissue is

lowered; inflammation, repair, and hypertrophy, on the other hand, are to be classed as progressive reactions.

CLOUDY SWELLING.

The simplest form of degeneration is the so-called cloudy swelling, which is best observed in the renal and hepatic epithelium and in the heart muscle. The organs are slightly enlarged, are pale and cloudy on section, and have a parboiled appearance. The cells or fibres swell and assume a granular and cloudy appearance, their nuclei being indistinct or refusing to stain. These changes are observed in most of the infections, *e.g.* scarlet fever, diphtheria, typhoid fever, septicæmia, smallpox, and erysipelas; but also in many other lesions and intoxicative processes, such as acute yellow atrophy, acute Bright's disease, and phosphorus poisoning, and are the expression of the deleterious action of certain toxic substances which alter the albuminous or protoplasmic constituents of the cells, producing a kind of intracellular coagulation. The change may go on to coagulative necrosis, the cell breaking down and being completely destroyed; it may survive, undergoing, however, fatty degeneration; or may recover completely. Injury to the cells and insufficient food supply are also common causes of cloudy swelling; thus in cardiac disease and marasmus the renal epithelium becomes cloudy. Inflammation, whether due to chemical, physical, or bacterial agencies, by injuring the cell directly or indirectly, will produce cloudy swelling. Virchow believed that the cloudy swelling in the early acute Bright's disease was the evidence of increased cellular activity on the part of the renal cells, and this he regarded as the sign and essence of the parenchymatous inflammation, wherefore this disease has been called parenchymatous nephritis. It is, however, held by some that cloudy swelling is a sign of degeneration, due to the pressure exerted on the renal parenchyma by the inflamed interstitial tissue and the inadequate nutrition of the cells, resulting from the stagnation of blood in the inflamed areas.

FATTY CHANGES.

Fatty changes are observed in the tissues and organs in many diseases and under the most varied conditions. Although they are as a rule the effect of a general lesion, it is obvious that they themselves must produce disturbances and impairment of function, and may become the starting-point or cause of other lesions and morbid states. Before discussing the nature of fatty changes, it will be advisable shortly to state the varieties of fatty changes as they are usually met with in the body.

Accumulation.—An increase of fat may take place in situations where it normally exists, *e.g.* (*a*) in the panniculus adiposus; (*b*) in the omental tissues; (*c*) in the epicardium; (*d*) in the bone marrow; and (*e*) in the liver, where, at certain periods after the ingestion of food, fat is always found.

Such accumulation may be—(1) temporary or transient, as for instance in the athlete who is "beefy" and out of training—it is then hardly pathological; or it may be (2) permanent and lasting, when it is morbid. Thus in obesity or lipomatosis, there is always a considerable storage of fat in the subcutaneous and omental tissues, and the liver of a beer-drinker is generally exceedingly fatty. The accumulation obviously must be due to one of two processes, or probably to both

of them. Either the supply of fat-forming material is in excess, too much fat being formed by the cell; or the fat formed is not split up as quickly or completely as it should be, owing to the exhausted condition or altered nutrition of the cells. It is evident that when the accumulation is excessive or too persistent, the functions of the fat-laden organ or tissues may gradually become impaired, and therefore, if the causes which in the first instance led to the fatty changes prevail, the process of combustion or splitting up of the deposited fat will also be interfered with; a vicious circle is thus established. Impairment of the cell function leads to fat accumulation, the latter increases the interference with the cell function, and so on. The statement that the accumulation of fat is due either to overproduction of fat or to failure of combustion, or to both, is merely a suggestion of what is obvious; it is no explanation of the process. Why should fat be stored up in some people and not in others living under the same conditions, why should obesity be commoner amongst women than amongst men? Some people "run into fat" on any diet, whatever they may do to keep their flesh down; others it is impossible to fatten.

It is difficult to state in concise and definite terms the causes of fat accumulation, but attention must be drawn to some leading, or it may be predisposing factors. Amongst these are—(a) inherited or congenital tendencies; (b) certain habits of life, such as indolence and sedentary occupations; (c) errors of diet; (d) chronic poisoning (e.g. alcohol); (e) sex, and diseases and morbid states of the reproductive organs in women; (f) morbid states of the liver, pancreas (?), or thyroid gland (?).

A truly morbid accumulation of fat is progressive. Any exaggeration of ordinary physiological conditions, due to errors in living, eating and drinking, may be set right again by correcting these errors.

Encroachment.—An extension of fat into tissues which normally are free from it may occur—(a) in the intermuscular tissues of the heart, spreading thither from the epicardial fat; (b) in the interstitial tissue of skeletal muscle (pseudo-hypertrophy); and (c) in the endocardial connective tissues.

In the fatty heart (lipomatosis) of an obese person there is first an accumulation of epicardial fat, whence it spreads between the muscle fibres, especially of the right ventricle, often reaching the connective tissue under the endocardium.

These two conditions are generally included under the single term *infiltration.* They commonly occur together in the same organ, and in the same individual they may affect one organ alone, or all the organs and tissues capable of undergoing fatty changes. Fat accumulation may be so localised as to produce a distinct tumour—a lipoma. In all these conditions the fat is, as a rule, collected in the cell in the shape of large drops or droplets, the nucleus being pushed to one side; the cell substance or protoplasm is sound, and after disappearance of the fat shows no defects.

Degeneration.—This differs from fatty accumulation, in which the fat is formed in the cell and stored up by it, in so far that *the fat is formed at the expense of the cell albumin.* Here the cell substance contains globules or numberless small granular droplets of fat, often so densely packed as to hide the nucleus or obscure the structure of the cell, the protoplasm of which is destroyed; on dissolving out the fat the cell appears vacuolated. Fatty degeneration is therefore a destructive process, a metabolic metamorphosis. It is best studied in the cardiac and voluntary muscles, in the liver cells and renal epithelium, in pus cells, and in nervous tissues.

The causes of fatty degeneration are those which produce serious disturbance of the nutrition or vitality of the cells. Amongst these are—(a) changes in the blood and nutriment supplied to the cells, as, for instance, in diabetes and various forms of cachexia; (b) vital depression and asphyxia of the tissues, e.g. venous engorgement, inflammation, pressure, fever, and starvation; (c) local and general anæmia, e.g. hæmorrhages, leukæmia, pernicious anæmia, and carbon monoxide poisoning; (d) intoxications, which include—(1) Bacterial intoxications (infective fevers, such as diphtheria, pneumonia, etc.); (2) intoxications by inorganic or organic chemical poisons, such as phosphorus, arsenic, carbolic acid, corrosive sublimate, and alcohol; (3) so-called auto-intoxications (e.g. acute yellow atrophy); (e) nervous lesions, which may lead to fatty degeneration in the muscles; (f) disuse of the muscles from whatever cause; (g) fatty accumulation and infiltration.

The extent of the fatty degeneration varies with the condition producing it. Thus a local anæmia, circumscribed pressure, or a focal inflammation can only produce a limited area of degeneration. Given a general cause, certain organs are more predisposed to it than others, as for instance the liver, heart, and kidneys; but one organ may be affected whilst others escape, although the cause be a general one. Thus, in leukæmia, the heart shows the fatty degeneration more strikingly than other organs; it may be the part solely affected. In a single organ, the degeneration, again, may be general or local, as in the kidney.

As to the process of degeneration in the cell, our knowledge is very limited; Gautier's view is that, under physiological conditions, the cell passes through two phases—(a) one of hydrolysis, during which the protoplasm is changed into urea and its allies, and the carbohydrates are converted into fat. This is followed by (b) the second phase of oxidation, during which the sugars partly disappear, partly change into fat, the fats eventually being burnt up. Imperfect oxidation, therefore, would produce a change of the cell protoplasm into fat. Pavy, who holds that protoplasm is a glucoside, believes that through some ferment action the carbohydrate molecule of the proteid is converted into a fat.

Long-continued or excessive fatty accumulation may lead to fatty degeneration. In the heart, the fat which has extended into and accumulated in the intermuscular substance, exerts pressure on the muscular fibres, impairs their nutrition, and gives rise to fatty degeneration. Similarly, a liver or pancreas heavy with accumulated fat eventually degenerates, and in the case of the pancreas the glandular substance may disappear altogether. This is probably due to two factors—(a) the fat accumulation reacts deleteriously on the vitality of the higher structures; and (b) the agent which produces this accumulation is often a tissue poison (e.g. alcohol), which, first causing an accumulation of fat, still continues to act on the already impaired tissues, and so advances the degeneration. In the same way the continued consumption of carbohydrates must be harmful to liver cells already overloaded with fat.

The fatty changes in the more important tissues or organs are the following:—

In the heart there is (a) an increase of the epicardial fat, which may almost surround the whole heart; (b) this fat may spread into the myocardium, along the intermuscular tissue, and so to the subendocardial tissue; (c) this accumulation of fat may, by pressure, cause fatty degeneration of muscular fibres themselves; or (d) the degeneration of the myocardium may be primary, without any previous accumulation of fat between the fibres. It is then generally patchy, giving rise to the well-known "tabby-cat" striation, "thrush's breast" or "dead leaf" appearance often so well marked in the musculi papillares. Under the microscope the degenerated fibres appear granular, and innumerable minute droplets of fat take the place of the striation.

In voluntary muscles the changes observed are analogous to those met with in the cardiac muscle.

In the kidney the fatty changes are usually purely degenerative, and they generally accompany other lesions, such as so-called parenchymatous or interstitial nephritis. They may occur independently—for instance, as the result of phosphorus, arsenic, metallic, or carbolic acid poisoning, or as the result of anæmia, diabetes, infective fevers, or circulatory disturbances. They may be diffuse or focal, and in either case are generally restricted to the cortex. When focal—as *e.g.* in diphtheria—the looped tubules of Henle and secondary convoluted tubules are affected; when general, the degeneration spreads also to the large convoluted tubules, the Malpighian bodies, and even to the connective tissue. The fat droplets appear first in the part of the cell nearest the membrana propria; they then gradually invade the whole cell, and eventually the cell may break down completely and be cast off. The large globules of fat found distending the cells can scarcely be of this nature.

In atheroma of the aorta the branched cells of the intima are filled with innumerable droplets of fat, the nucleus being obscured, although itself often not degenerated.

Fatty changes in nerves are easily recognised in the so-called peripheral neuritis. The myelin sheath [1] breaks up into globules and irregular masses of fat, which stain intensely black with osmic acid, and analogous changes may be observed in the *cord* in cases of degeneration, whether ascending or descending.

Next to the heart, fatty changes have been most completely studied in the *liver*.[2]

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[1] Normal myelin is not stained black with Marchi's fluid (osmic acid solution in dilute Müller's fluid), although ordinary body fat (which is a neutral fat) does. The myelin has therefore been changed into fat.

[2] Kanthack follows Cohnheim, and does not use the term infiltration. He says: "The intestinal epithelium absorbs fat from the intestinal contents, and leucocytes and phagocytes take up fat granules from a degenerated area—these are the nearest approaches to an infiltration; it is, however, an ingestion, followed probably by assimilation and digestion. The fat appearing in the tissues under normal conditions, whether in the secreting mammary gland, in the liver, or in the panniculus adiposus, has been produced by chemical action, or by a fatty metamorphosis from the albuminous cell protoplasm; this cannot be called an infiltration. In fact, the physiological secretion of milk depends on a true, though partial, fatty degeneration of the cells lining the alveoli."

"Pathologists are in the habit of distinguishing between fatty infiltration and fatty degeneration in the liver; their criteria are partly anatomical, partly morphological. In fatty infiltration the globules are said to be larger, and arranged either at the periphery of the liver acini, or centrally around the intra-acinous vein, or in the interstitial tissue between the acini; while in degeneration the droplets are said to be small, to occupy the whole cell, and the metamorphosis is stated to be, as a rule, general. It is asserted that in the former case the fat has been stored up in the cell; in the latter, it has been formed at the expense of the cell substance. Most observers describe infiltration in obesity, nutmeg liver, phthisis, cirrhosis, and similar conditions on account of the anatomical distribution and morphological appearances of the fat. In obesity, at least in the early stages, there may possibly be an accumulation of fat without the cell suffering, the cell being over-active, and forming fat from the material generally supplied in excess; but it is difficult to understand how a true accumulation or infiltration could occur in diseases in which the fat disappears from the subcutaneous and omental tissues, *i.e.* in wasting diseases. In them the fat must have been formed in the cell, and at the expense of the cell, whether the appearances are those of infiltration or degeneration, as generally described. In the obese person the liver cells, after forming an excess of fat, are capable of replacing the cell albumin which has been used up in the manufacture of fat, and only when they cease to do this will degeneration also appear. As Cohnheim puts it, the guiding rule of distinction between degeneration and infiltration, or, as I prefer to say, accumulation, is this: 'Does the fat occupy a cell with diminished or normal albuminous contents?' In the early stages of obesity there is merely an accumulation of fat in the 'legitimate localities'; in the later stages this becomes excessive, and the fat extends beyond these localities, and, as far as the liver is concerned, instead of being restricted to the periphery of the lobule, occupies the whole of it, producing a large, fatty liver." The accumulation of fat in this case is probably due to the two factors mentioned previously, namely, incomplete oxidation and excessive supply of the precursors of fat; it is not, to begin with, an atrophy, although eventually this also may follow in some of the organs (*e.g.* heart and liver). He agrees with Cohnheim that the fatty changes observed in the liver with anæmia, phthisis, cancer, etc., are all

The true accumulations—or infiltrations, to use the more familiar term —are—(a) the normal physiological storage of fat; (b) the transient accumulation in persons of sedentary habits; and (c) all but the most advanced stages of obesity. Other conditions are atrophic, and are associated with fatty degeneration. There are undoubtedly two varieties of fatty degeneration. In one the destruction or disintegration of the cell albumin is rapid and excessive, and the cells break down quickly, as for instance in acute yellow atrophy, phosphorus and arsenic poisoning; in the other the cell destruction goes on more slowly, and the fat formed at the expense of the cell substance has a chance of accumulating for a long time (e.g. phthisis, anæmia, cachexia). Local fatty changes in the liver are also atrophic, and may be produced by pressure of tumours, or by the contraction of newly formed fibrous tissue.

Termination.—An *accumulation* may either disappear by oxidation and resorption on change of habits, or it may pass on to degeneration. *Degeneration,* especially if local, may be repaired by restitution of the tissues (e.g. in muscles and nerves), the fat granules being removed by phagocytosis or oxidation; or it may end in complete disintegration, death, and necrosis, the fat then being replaced by fibrous tissue, e.g. sclerosis of voluntary muscle or of the nervous tracts in the cord, in accordance with the law that "degenerate tissue, if not regenerated, is replaced by connective or fibrous tissue."

AMYLOID CHANGES.

In amyloid disease curious deposits make their appearance in certain tissue elements. When these are extensive, they are not unlike boiled starch, and the tissues are transformed into glassy or hyaline masses. Amyloid deposits can be readily demonstrated by the following chemical reactions:—(a) A solution of iodine stains amyloid a deep mahogany-brown; if a weak solution of iodine be allowed to act for a long period, and sulphuric acid be added, a bluish or violet colour may sometimes be obtained. From this modified starch reaction the name "amyloid" was derived. (b) Methyl-violet stains the amyloid material red, leaving the other parts bluish. The reaction is best marked if, after staining with methyl- or gentian-violet, the tissues be washed in water, acidulated with hydrochloric, oxalic, or acetic acid. It must be remembered that other substances, such as "colloid" and "hyaline," occasionally stain somewhat like amyloid; everything that gives a red reaction with methyl-violet must not be regarded as amyloid. According to Lubarsch, the methyl-violet test is convincing (a) wherever iodine or iodine-sulphuric acid gives a positive reaction; (b) in the absence of the iodine or iodine-sulphuric acid reaction wherever the substances which stain red with methyl-violet optically, chemically, and topographically agree with genuine amyloid; or (c) wherever it appears under conditions which are generally associated with amyloid degeneration.

true fatty atrophies, whatever they may appear to be on histological rules, more or less arbitrarily laid down. "In phthisis," Kanthack continues, "the fat is often found in large drops at the periphery of the hepatic lobule, and many describe this as infiltration or accumulation without degeneration. They believe that the excessively fatty liver of emaciated consumptives is due to an infiltration with fat, which has been formed elsewhere during the process of wasting. How can this be? The fat must have been formed at the expense of the cell substance, and it remains *in situ* on account of diminished combustion. The fatty changes of starvation are also certainly atrophic."

Amyloid, though a proteid, does not react like an ordinary albumin, and resists digestion. It is asserted, however, that in a finely divided condition it undergoes both peptic and tryptic digestion; it is dissolved on heating in water or alkalies.

Causation.—(1) The commonest cause is chronic suppuration, and especially that accompanying chronic pulmonary phthisis, tuberculous disease of the bones and joints, syphilitic bone disease; ulcerating cancers and varicose ulcers of the legs are also given as causes; (2) tuberculosis and syphilis (especially in the tertiary or congenital form) without concomitant suppuration; (3) actinomycosis; (4) Bright's disease; and (5) various forms of grave anæmia and cachexia may also lead to amyloid disease.[1]

If the various lesions with which amyloid changes may occur be reviewed, it will be found that the common factors are—(1) continued loss of albumin, producing chronic anæmia, or marked hydræmia; and (2) the incidence or intercurrence of infective processes, often secondary, such as suppuration of bone, or in connection with ulceration.

Localisation.—In general amyloid disease, certain organs, the liver, spleen (oftener than any other organ), kidney, suprarenal capsules, lymphatic glands, and intestinal mucosa, especially that of the large intestine, are more especially selected, and, as a rule, several of them are simultaneously affected.[2]

Most of the attempts to produce amyloid disease experimentally have been negative, but a few positive results have been recorded. Czerny kept up a chronic suppuration in dogs by means of turpentine and nitrate of silver injections, and found that the spleen and liver invariably showed amyloid changes. Examining the pus corpuscles and leucocytes, he found that during the experiments they showed granules which stained dark brown with iodine, and turned blue on the addition of sulphuric acid; he assumes that this substance is preamyloid matter, which is carried by the leucocytes to the tissues, deposited there, and then changed into amyloid. Similarly, he found that during suppur-

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[1] In 269 cases Birch-Hirschfeld found amyloid changes—

							Times
In spleen alone	.	.	.	.	.	.	35
„ liver „	.	.	.	.	.	.	2
„ kidneys „	.	.	.	.	.	.	1
„ spleen, liver, and kidneys	.	.	.	.	.	.	142
„ spleen and kidney	.	.	.	.	.	.	77
„ spleen and liver	.	.	.	.	.	.	10
„ kidneys and liver	.	.	.	.	.	.	2

[2] Birch-Hirschfeld has analysed 262 cases, and in these there were present—

				Times.
1. Chronic tuberculous disease of the lungs	.	.	.	140
2. Pulmonary phthisis and bony tuberculosis	.	.	.	21
3. „ „ intestinal tuberculosis	.	.	.	18
4. „ „ syphilis	.	.	.	2
5. Bony tuberculosis alone	.	.	.	28
6. Chronic suppuration of bone (non-tuberculous)	.	.	.	4
7. Syphilis (gummatous, especially in liver)	.	.	.	15
8. Cancerous ulcers	.	.	.	5
9. Varicose ulcers of leg	.	.	.	3
10. Visceral suppuration	.	.	.	8
11. Actinomycosis	.	.	.	1
12. Noma	.	.	.	1
13. Peritoneal tuberculosis	.	.	.	4
14. Chronic arthritis	.	.	.	1
15. Suppurative cystitis and pyelitis	.	.	.	1
16. Doubtful causes	.	.	.	10
				——
				262

ative processes in man pre-amyloid substances appear in the leucocytes, and he concludes that the precursors of amyloid are formed in the pus—whether micro-organisms are present or not is immaterial; that they are diffused or distributed in the various organs and deposited there as true amyloid; and that this deposition shows itself first in the spleen.

Krakow made repeated inoculations into rabbits and other animals with pure cultures of the *Staphylococcus pyogenes aureus* until they showed marked wasting; he thus produced amyloid changes in their organs, which also began in the spleen, and in every detail agreed with what is observed in man, microscopically and histologically.   He believes that microbic infection is absolutely necessary.   Other observers have failed to obtain results similar to those obtained by Czerny and Krakow.

Processes.—How is the amyloid substance deposited in the tissues? There exist two conflicting views—(1) that the amyloid is produced *in situ* by the cells from their albuminous constituents—degeneration ; (2) that it is formed in the blood and carried to the tissues—infiltration. It is generally accepted that amyloid matter appears in the interstitial tissue only, never in epithelial cells, although such excellent observers as Dickinson and v. Recklinghausen spoke, and the latter still speaks, of intercellular and intracellular infiltration.   Most pathologists hold that it is exclusively the connective tissue which contains the amyloid, whether it be deposited there by a process of degeneration or by infiltration.   If Czerny's observations be accepted, the amyloid change is an infiltration.   Against this is the fact that amyloid has never been observed in the blood.   It is undoubted that amyloid appears first in the intercellular substance.   It has been stated by some observers that in the liver the amyloid is deposited first in the hepatic cells (Dickinson) ; but others, and especially more recent observers, emphatically deny that these cells ever show amyloid changes, and that amyloid changes ever occur in (*a*) epithelium, (*b*) striped or unstriped muscular tissue, or (*c*) leucocytes, but that the deposition is always an interstitial one, and that the tissue cells degenerate through pressure exerted by the amyloid tracts.

Amyloid changes during the earliest stages are most frequently observed in or along the capillaries and smallest arterioles.   Their walls become swollen, and their lumen narrowed ; in the arterioles the amyloid matter is deposited in the middle coat, the muscular elements remaining intact, the material appearing in the connective tissue ; in the capillaries it is deposited in the interstitial substance of their walls.   From these points the amyloid change extends into the surrounding tissues, implicating the connective tissue and the basement membranes.   In the liver and kidney the epithelial cells outside the amyloid tracts alway show marked fatty degeneration, and those within these tracts disappear altogether ; and when vital organs are concerned, the final results must be anæmia, hydræmia, marasmus, and death.   The amyloid matter not only presses on the cells, but also narrows the lumina of the vessels; vascular obstruction is produced, which, if arterial, still further impairs nutrition and function ; and, if venous, may lead to œdema and dropsy.   Thus, in amyloid disease of the liver, ascites, due to portal obstruction, is common ; in amyloid disease of the kidney, albuminuria not unfrequently occurs.

Terminations.—Is amyloid substance, once formed, ever reabsorbed ? Litten attempted to answer this question experimentally by placing fragments of amyloid tissue in the peritoneal cavity of the rabbit ; what was left of the amyloid tissue no longer gave the methyl-violet reaction.   It is known that wandering cells may ingest amyloid matter.   There is some clinical evidence that occasionally an amyloid liver may diminish in size.

'It must, however, be remembered that the clinical diagnosis is by no means always certain.

In the liver the amyloid is early deposited along the capillary walls in the intermediate or hepatic zone of a few lobules, compressing the liver cells, which themselves, however, remain otherwise unaffected, and the naked-eye appearances are almost unchanged; later, the liver becomes enlarged and firm, smooth, and almost opalescent on section. The degeneration affects specially the intermediate portions of the acini. Such as are left of the liver cells must be looked for at the extreme periphery or the extreme centre of the lobule; those at the periphery are almost always in a state of fatty degeneration. In the amyloid zone nothing is found of the cell outlines; the cells have vanished, or only the merest remnants are found. .

(a) *In diffuse amyloid spleen*, usually associated with heart disease, the sinuses and capillaries are surrounded by amyloid tracts, which also extend along the reticulum, gradually compressing the spleen cells, and pressing upon the follicles, which are unaffected except in many cases as to the central vessel.

(b) *In sago amyloid spleen*, the capillaries and reticulum of the follicles become amyloid; the lymphocytes eventually may disappear altogether through pressure. The central vessel is seldom affected, and then at a late stage of the disease.

In the kidneys the amyloid changes are best observed in the cortex, but are present also in the medulla. In the cortex, the glomeruli, membranæ propriæ, arteries, and capillaries are affected, and in the medulla the vessel walls and membranæ propriæ, but, as stated by modern observers, the renal epithelium seldom or never suffers. The glomeruli become enlarged and transparent, and filled by amyloid capillary loops; the nuclei of the glomerular epithelium disappear.

Intestine.—The amyloid changes are observed in the walls of the vessels of the villi, mucosa, and submucosa, and in the reticulum of the villi.

Lymphatic glands.—The capillaries and reticulum become amyloid, and appearances resembling those described in the spleen are seen.

Occasionally amyloid changes may appear locally, as in the conjunctiva and in the connective tissue, or in tumours. These require no special description or discussion.

HYALINE AND WAXY DEGENERATION.

Under certain conditions hyaline masses, transparent, homogeneous, and bright in appearance, are met with in the organs and tissues. Hyaline is not a definite chemical substance, but includes bodies all of which are characterised by their great resistance to water, alcohol, acids, and ammonia, and their affinity for acid aniline dyes, such as acid-fuchsin and eosin; von Recklinghausen includes hyaline, mucous, and amyloid changes under colloid metamorphosis, but this is misleading. Klebs restricts the terms colloid to all hyaline substances derived from epithelium and hyaline to similar substances derived from connective tissue; this seems to be the safest classification, although it indicates but roughly the chemistry of these bodies.

Certain authors maintain that there are two varieties of hyaline—(a) that secreted by the connective tissue cells (*i.e.* of intracellular origin); and (b) that produced by coagulation of plasmatic fluids, serum, plasma, or lymph (*i.e.* of extracellular origin). It is best to agree with Birch-Hirschfeld that intracellular hyaline formation is merely a form of so-called coagulation necrosis, and that hyaline degeneration is due to a coagulation of fluid derived from the blood plasma, muscle plasma, lymph or cell plasma.

Hyaline changes may be hæmatogenous, as in thrombi in the capillaries, especially in infective diseases; or exudative, when a diphtheritic membrane becomes hyaline; or when, in chronic Bright's disease, the albuminous casts become hyaline. The muscle substance in some cases, especially in infective fevers (*e.g.* typhoid and diphtheria) may break up into hyaline transparent masses, no doubt due to a coagulative change in the muscle plasma. This condition is frequently spoken of as *vitreous degeneration*, and may be caused also by injury, chemical, physical, or mechanical, to the muscle. The fibres break up inside the sarcolemma into irregular hyaline masses which swell, and as a rule are broader than the unchanged fibres. On microscopic examination the muscle has a cloudy or boiled appearance. Fibrin, which itself is a product of coagulation, may become hyaline, as frequently observed in croupous pneumonia, in thrombi, and in the walls of aneurysms.

Hyaline changes must be regarded as the result of coagulative processes, all the more that they are generally observed in inflammatory lesions, or where there has been an increased exudation. The vessel wall or surrounding connective tissue or muscle substance imbibes some kind of fluid which coagulates. Some writers believe that hyaline is closely allied to amyloid, because hyaline degeneration may be an antecedent condition; hyaline and amyloid changes are often found together, and there is a gradation in staining reactions from amyloid to hyaline; hyaline changes are common in and around the capillary or arterial vessel wall, and amyloid changes always begin there; lastly, infective processes are common causes of both forms of degeneration.

COLLOID CHANGES

These are allied to mucous and hyaline degeneration. Colloid differs from mucin in that it is not precipitated by alcohol and acetic acid. It is a gelatinous hyaline substance and is always of epithelial origin. Many changes are frequently described as colloid which are not of this nature. Physiologically colloid appears in the follicles of the thyroid gland, and if, as in goitre, the production of colloid becomes excessive, the condition becomes pathological. In tumours also (carcinoma) colloid may be formed, the cells becoming distended with globules and masses of colloid which they discharge, while they themselves may be entirely destroyed. It is doubtful, however, whether the so-called colloid cancer is really colloid, and not rather myxomatous. In interstitial nephritis colloid cysts are frequently found, though some writers are inclined to regard their contents as produced by coagulation of an albuminous substance, and therefore as being allied to hyaline.

MUCOUS CHANGES.

Mucin is a transparent viscid colloid substance, the chemical nature and properties of which are as yet insufficiently known. According to Landwehr, it is a compound of albumin with a carbohydrate body called animal gum, which on boiling with dilute mineral acids (sulphuric acid) yields a non-fermentable sugar. The mucin produced by epithelial cells differs materially from that derived from connective tissues, whilst again the mucin obtained from epithelium is not a constant substance. Thus the mucin found in ovarian cysts is not precipitated by acetic acid, while that formed by the columnar cells of the intestines is solidified by both alcohol and acetic acid.

Under pathological conditions, mucin may show itself (*a*) as a product of abnormal epithelial activity. The columnar cells of mucous membranes normally form mucin in a mucous catarrh the number of goblet cells becomes much

increased, or every columnar cell may be distended with mucin. Again, the columnar cells lining the cystic spaces of an innocent tumour (such as an ovarian cyst), or of a malignant tumour (such as a columnar-celled carcinoma), may also produce an excessive amount of mucin, so that the cystic spaces become distended with mucus. On the other hand, (*b*) mucin may appear in connective tissue, bone, cartilage, and fat, or in the connective tissue tumours. There is then either a viscid gelatinous matrix, embedded in which are numerous reticular cells, or a more or less dense network of filaments (a reticulum). In myxœdema, in certain stages of the disease, the connective tissue of the skin becomes gelatinous. It must be remembered that embryonic connective tissue is myxomatous, and that, therefore, young connective tissue appearing under morbid conditions is also frequently mucous.

WASTING AND ATROPHY.

Atrophy, closely allied to degeneration, is a condition in which there is diminution in the size of an organ or part, or even a cell of the body. This is a purely morphological term, and was originally used to indicate macroscopic changes. When a liver rapidly decreased in volume, as the result of marked fatty degeneration, the process was called an acute atrophy; but from histological observation it is now known that this is a degeneration followed or accompanied by necrosis, and not an atrophy proper. Arrested development (hypoplasia) must not be confused with atrophy, for here the organ has never attained its normal size. Hypoplasia may be due to intra-uterine changes, or it may be caused by forces acting at the seat of and during the period of growth, as in microcephalus, undeveloped thyroid, and stunted epiphyses of long bones following rickets or inflammation. After an amputation of a leg, during childhood or youth, the corresponding side of the pelvis remains small, whilst infantile paralysis of the upper extremity leads to arrested development of the clavicle and scapula on the same side. When development has not taken place at all, the term aplasia or agenesis is used.

Atrophy of an organ must be due (1) to diminution in the size of the component elements, (2) to a diminution in the number of these elements, or (3), and most commonly, to a combination of the two. At the same time, inadequate regeneration may play a most important part in this condition. Under physiological conditions cells continually disappear, but they are replaced by others. If, however, the regenerative process does not at least balance the normal decay, the part must diminish in size, *i.e.*, it must undergo atrophy, as when tissues become senile, *e.g.* the skin and the muscles of an old man are visibly atrophic, although there is no degeneration; a cell, having played its part, disappears from the scene, and its place is not filled by another cell, —simple atrophy. In the atrophy of degeneration, on the other hand, the cells become fatty, hyaline, amyloid, or necrotic, and are then removed as dead matter or are replaced by fibrous tissue; the part becomes smaller and many cells disappear, the diminution being due to degeneration and death, and the removal of the useless material. It may be held that as decayed tissue is replaced by fibrous tissue, which, contracting still further, diminishes the size of the organ, it is quite unjustifiable to speak of atrophy. The shrinkage in an atrophic cirrhosis of the liver, or an atrophic red kidney, is due to the condensation of the fibrous tissue, and it might be better to speak of a shrinking liver, and a shrinking or

contracting kidney. On examining such a shrinking organ, *e.g.* kidney, it will be found that many of the epithelial cells pressed upon by the fibrous tissue become smaller and smaller, *i.e.*, they atrophy, till eventually they degenerate, die, and are cast off.[1]

Simple atrophy may be observed—(1) under physiological conditions, *e.g.*, when the thymus gland gradually disappears ; (2) as a senile change ; or (3) it may be due to morbid conditions, *e.g.*, when, on account of diminished nutrition, an organ or a tissue becomes reduced in size. Thus during inanition the fat atrophies, the muscle becomes smaller, and the glandular cells disappear, there being in all three cases an impairment of regeneration on account of the inadequate food supply. It is doubtful whether the disappearance of the fat can be called an atrophy, except in the sense that it is not regenerated. Just as the plant stores up starch for future consumption, so does the animal body store up fat ; the using up of the fat is not atrophy, but the adipose cushions vanish, because there is no regeneration. The diminution of nutrition may be due (*a*) to general causes, such as starvation, or (*b*) to local circulatory disturbances or local pressure, but in the latter case there is also, as a rule, actual destruction of the cells by continued pressure.

In morbid conditions "simple" atrophy is rarely met with. When a paralysed muscle wastes, it generally becomes fatty, or is replaced by fibrous or fatty tissue, and similarly in starvation the cells in the wasting organs often undergo degeneration. Indeed, true and uncomplicated histological atrophy is rare ; either degeneration or fibrosis is also present, or the two processes may be combined. Atrophy, in the generally accepted sense of the term, is usually accompanied or preceded by degeneration, and may be due to shrinkage of newly formed tissue.

Atrophied tissue may be restored, as where a wasted muscle again increases in bulk ; in which case an active regeneration more than balances the normal loss. But if repair does not take place, then the muscle degenerates or dies ; should "repair" occur after this, as it may, it must be either by new proliferation of homologous cells, or by the formation of fibrous tissue. (See "Chronic Inflammation.")

NECROSIS AND NECROBIOSIS.

Death of the tissues may be—(*a*) *Gradual* (necrobiosis), when it is usually preceded by a chronic degeneration, such as fatty degeneration or a more acute form of degeneration, such as cloudy, hyaline, or coagulative changes, nothing of the original shape, form, or structure of the tissue being left. In tuberculosis and syphilis, and even in carcinoma and sarcoma, it is generally maintained that a process of so-called coagulative necrosis, which is closely allied to cloudy swelling and to the hyaline or waxy changes, is first set up. The cell protoplasm becomes solid or coagulated, granular or hyaline, the nucleus disappears or becomes obscured, and both cell and nucleus refuse to stain. If this intracellular coagulation is followed by a breaking up of the cell into detritus or fatty débris, then the result may be caseation. Caseation, however, is quite independent of fatty metamorphosis, and may occur without it. Caseous matter, as a rule, is semi-solid or pultaceous, whitish or yellowish in colour, microscopically granular, staining indefinitely, or not at all (in certain stages of the process hæmatoxylin gives a very deep stain) ; it becomes dry and cheesy ;

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[1] Kanthack held that in a shrinking organ, cellular atrophy may be observed under the microscope, but that the shrinkage is not atrophy. It is well to remember, however, that atrophy is a mixed process, and received its name before pathological histology existed.

it is dead matter, and therefore becomes easily calcified, and if present in any quantity cannot be absorbed, but must be removed, either by operation or by ulceration.

Death of the tissues, on the other hand, may be—(b) *Acute or sudden* (necrosis), the tissues retaining their form for some time, and must be the result of either (1) a gross or fatal tissue injury, or (2) starvation of the tissues, due either to want of food or incapacity on the part of the cells to assimilate the food supplied. Thus a direct injury, *e.g.* a crush, a burn, or a caustic, may destroy cell life immediately, or it may lead to serious inflammation, which only later brings about the death of the part. Again, if the nutrition of the cell is suspended it must die, as when there is a complete or serious obstruction to the circulation, (1) arterial, (2) venous, or (3) capillary. Thrombosis, embolism, or obliterative endarteritis may produce gangrene or necrosis, *e.g.* dry gangrene in the extremities, cerebral softening, infarctions. Complete venous obstruction, as for instance in a strangulated hernia, may cause absolute stoppage of the circulation, *i.e.* capillary stasis, which, if not relieved, must result in death of the part. A complete capillary stasis may also be produced by inflammatory pressure, due to the accumulation of exudation; in dense hard tissues, as in bone, this often leads to necrosis.

It is evident that an injury leads to necrosis partly by favouring or producing inflammation, which in its turn favours capillary stasis, and partly by impairing the vitality of the cells directly, so that comparatively slight causes are sufficient to extinguish life altogether. It must further be remembered that in many forms of gangrenous or necrotic inflammation, such as diphtheria, cellulitis, phagedæna, etc., bacteria are concerned; they keep up a continual supply of tissue poisons, which not only have a deleterious action on the cells themselves, but also excite the surrounding tissues to inflammation. A vicious circle is thus established; the bacterial irritants predisposing or weakening the tissues, which then succumb readily to the inflammatory pressure, which latter in turn predisposes the tissues to the action of the bacterial poisons. Weakened or predisposed parts become necrosed more readily than vigorous and healthy ones, and causes which under normal conditions would only produce an inflammation or a transient retrogressive change, may be severe enough to destroy a debilitated organ or group of cells. Thus an incomplete arterial obstruction may cause gangrene in an individual suffering from cardiac disease, or in the old and exhausted; necrosis of the bone is commoner in those who suffer from infective fevers, and infective emboli are more serious than simple ones. Chronic alcoholism predisposes to gangrenous cellulitis; diabetes, anæmia, marasmus, general weakness, and a feeble circulation are also all powerful predisposing factors; the tissues are already badly nourished under such conditions, and but little suffices to destroy life altogether. Sometimes the predisposing factors may be local, such as atrophy or serious lesions. Paralysis and anæsthesia are not direct causes of necrosis, but they favour its occurrence no doubt by influencing the nutrition of the part.

Gangrene and necrosis, therefore, are due to (a) a cutting off of nutrition from a part, (b) changes which exclude the assimilation of what is supplied, (c) predisposing causes, intensifying the effect of the two processes mentioned. Generally speaking, it may be said that the first change is a coagulation of the protoplasmic cell contents, *i.e.* a coagulative necrosis. If no moisture is supplied, or if that which exists is absorbed or evaporates, the result is a dry gangrene or mummification, but if the part is moist from œdema, whether passive or inflammatory, then a moist gangrene or colliquative necrosis results.

The dead or dying tissues may putrefy if bacteria find an abode in them, and these bacteria may themselves cause a liquefaction of the decomposing matter.

Thus there may be distinguished—(1) dry gangrene, due as a rule to an obstruction or weakness of the arterial circulation; (2) moist gangrene, which is due either to the same causes, œdema existing or appearing at the same time, or has its origin in a severe inflammatory condition; (3) traumatic gangrene, which includes (*a*) immediate death as the result, for instance, of a crush, or (*b*) inflammatory necrosis (cellulitis and phagedæna), or (*c*) special infective forms, such as noma, cancrum oris, acute spreading gangrene, or emphysematous gangrene, or rapid septic gangrene, or necrosis; (4) symmetrical or idiopathic gangrene, the etiology of which is at present but little known; (5) gangrene accompanying infective fevers, such as ulcerative endocarditis, typhoid fever, etc.; (6) the gangrene of anæmia and marasmus; and (7), most obscure form of all, the gangrene of nervous origin, *e.g.* hysteria and Raynaud's disease. Any form of ulceration, or sloughing inflammation, bedsore after hæmorrhagic extravasations, from pressure or during œdema, or abscess, is accompanied by necrosis, which, however, may be so small as to escape detection with the naked eye.

In bones the death of the tissues shows itself either in the form of an extensive necrosis,—a sequestrum, or as caries. In the intestinal tract, gangrene of the bowel is observed in cases of hernia, intussusception, and strangulation; necrosis occurs in the various forms of ulceration, such as are seen in typhoid fever, ulcerative colitis, and dysentery; while in the pharynx and larynx, diphtheria offers the commonest example of necrosis. In the lungs large areas may become gangrenous, as for instance during or after pneumonia; or as the result of the presence of a foreign body or an injury. Necrosis is observed with caseation or during the development of cavities in the lung. Sloughing and necrosis also occur in new growths, especially in those of a malignant type, of the bladder and uterus, liver and pancreas. The so-called fat necrosis, in which the omental and mesenteric fat more especially shows numerous dull white or yellowish areas, consisting of dead, solid, or saponified fat, generally accompanies sloughing or inflammation of, or hæmorrhage into, the pancreas.

Necrosed tissue must be removed from the body, and whatever defect remains is subsequently made good by newly formed fibrous tissue, unless the necrosis was slight and superficial, when there may be homologous repair, as for instance when epithelium is cast off and the gap is filled by epithelium.

CALCIFICATION AND CONCRETIONS.

Calcareous changes generally appear in dead or dying tissues, never in perfectly sound and normal structures. Two main processes may be distinguished—(*a*) infiltration and (*b*) concretion.

Infiltration.—The deposition of calcium phosphates and carbonates, often with similar magnesium salts, occurs either in the cells or in the matrix binding the cells together; these salts occur first in the form of minute granules which are soluble in hydrochloric acid, often with an evolution of gas if carbonate be present. The granules are readily stained by hæmatoxylin, and gradually fuse into homogeneous masses which may have a concentric arrangement.

Forms of calcareous infiltration.—(1) Normally it is observed during the formation of bone, when the lime salts may be deposited either in the cartilaginous

matrix or in the dense osteoid connective tissue substance. (2) It occurs in senile tissues, notably in cartilage, *e.g.* the laryngeal or costal cartilages, which may even ossify; and in the vessel walls, especially in the intima or media, where it is generally preceded by a morbid lesion, such as atheroma or fibrosis, the tissue being in an impoverished condition on account of a weakened circulation. (3) In continually irritated or hyperplastic connective tissue, the result of so-called chronic inflammation. Thus in a thickened pleura or in tendons of muscles constantly exposed to pressure (*e.g.* from riding), calcareous changes are not rare, and in the adventitious fibrous capsule produced by the continued irritation of parasites, as in hydatid and trichina cysts; in this, subsequently, lime salts are deposited. (4) In tumours, such as fibromyomas or growths containing cartilage, calcareous changes are by no means uncommon. When cartilage is present, the process is almost physiological, while in the fibrous tumours those parts suffer which are furthest removed from the blood supply, or which, for some other reason, have their vitality impaired. (5) Calcareous changes are especially common in caseating or necrosed tissues, and wherever fibrin is present, as for instance in thrombi, infarcts, or endocarditis. Hyaline changes are also very common precursors of calcification. Generally speaking, then, calcareous infiltration occurs in connection with a dense matrix or tissue, dead or necrosing elements, and with impaired nutrition; it is therefore intimately associated with degeneration and necrosis. Soluble calcium salts, lactate or glycerophosphate of lime in the blood, and lymph, may become converted into insoluble salts, the carbonate or phosphate; while at the same time there is a diminution in the amount of fluids keeping the lime salts in solution.

Concretions are calcareous or earthy masses occurring in pre-formed or pre-existing cavities, in the lumen of vessels, tubes, or ducts. They may be found in serous cavities, when they generally develop in fibrinous masses, or they may present themselves as calculi. In the latter case the lime salts are generally combined with other substances, and they may be altogether of secondary importance. Calculi are found in the kidneys, the gall bladder, pancreatic and salivary ducts, the prostate and urinary bladder; concretions may also occur in the intestine, veins, or tonsils, as enteroliths, phleboliths or rhinoliths, the development of which is generally accompanied by—(1) stagnation of the excretion or secretion; (2) a solid substance, it may be a small crystal, around which the incrustation or deposit takes place; (3) changes in the chemical constitution of the fluids and in their solvent power, which are often due to bacterial activity and to an increase of albuminous, mucous, or colloid substances. Gouty concretions, which consist of urate of sodium mixed with carbonate and phosphate of lime, will be considered elsewhere.

PIGMENTATION.

Pigment may be of little or no importance, or it may be of the greatest significance in the diagnosis of disease. The pigment may be exogenous, having entered from without, or it may be endogenous, derived from the body itself. Examples of the former process are anthracosis, where carbonaceous matter is stored up in the lungs or lymphatic glands, the liver, diaphragm, and other parts; argyria, where, as the result of continued ingestion of nitrate of silver, salts of silver are deposited in the connective tissue and vascular walls of the skin and kidneys; and tattooing, where insoluble coloured substances are rubbed into excoriated skin and its lymphatics, whence in part they are carried to neighbouring lymphatic glands.

Pigmentation.

I. *Exogenous*—	II. *Endogenous*—
Anthracosis.	1. Hæmatogenous $\begin{cases} \text{extravascular.} \\ \text{intravascular.} \end{cases}$
Argyria.	2. Overproduction.
Tattooing.	3. Atrophic.
	4. Hepatogenous.

Such conditions are of little pathological interest. In anthracosis of the glands the black pigment occurs in the larger connective tissue or endothelial cells, but never in the lymphocytes themselves; in anthracosis of the lungs the pigment is found in the epithelial cells of the alveoli, but chiefly in the interstitial connective tissue between the alveolar walls, where it lies in the same type of cell in the peribronchial or periarterial tissue (even media and intima may be affected), and on to the bronchial glands. The deposited pigment acts like other foreign bodies, and produces a hyperplasia of the connective tissue which becomes fibrous (fibrosis and induration). When the vessel walls are markedly infiltrated, they appear as rings of pigment. Anthracosis affects especially the bronchial, tracheal, cervical, portal, and mesenteric glands. Passing along the lymph sinuses, this pigment is taken up by their endothelium, and is at first deposited around the periphery of the lymph follicles. Its presence produces a fibrosis of the reticulum just as it did in the lung, and many of the newly formed connective tissue cells become impregnated with pigment; this gradually extends into the follicle, which becomes indurated, its lymphocytes disappearing before the proliferating endothelial or connective tissue cells. Tattoo pigments are taken up in the same manner. Where the pigment is of endogenous origin, it may have been derived (1) from the blood; (2) from overproduction due to an increased functional activity of the pigment cells; (3) from certain degeneration processes; or (4) from the bile.

Hæmatogenous pigmentation may be (a) *extravascular*, or (b) *intravascular*. In the former case it may result from a hæmorrhage or an engorgement, with diapedesis and destruction of the red blood corpuscles. The pigment is brownish or yellowish in colour, and consists either of hæmatoidin or hæmosiderin. Hæmatoidin is crystalline acicular, or rhombohedral and free from iron. It is apparently identical with bilirubin; but it includes several substances, all iron-free derivatives of hæmatin, which are formed in and by the tissues as opposed to the cells. Hæmosiderin, on the other hand, an iron-containing granular pigment, is manufactured in and by the cells themselves, which have taken up the destroyed red corpuscles. It may be taken to the lymphatic glands by the wandering cells. Hæmosiderin and hæmatoidin often occur together. (b) When the pigment is formed inside the vessels (1) the blood may be stagnating, and there may be a thrombosis, when a state of things corresponding to that existing in a hæmorrhage is present, or (2) the blood may be circulating. Certain poisons may cause a dissolution of the red corpuscles (a hæmolysis), the dissolved hæmoglobin being taken up by the blood plasma (hæmoglobinæmia), to be excreted by the kidneys as hæmoglobin (hæmoglobinuria), which may be present in such quantities that it may even cause a brown discoloration of the uriniferous tubules (hæmoglobin infarcts). Experimentally, hæmolysis may be produced by chlorate of potassium, arseniuretted hydrogen, and toluol-diamine, etc.

In other cases a living virus may attack the red corpuscles directly, as for instance in malaria, where an iron-free black pigment (melanin) appears in the spleen, liver, brain, and bone marrow, and is also deposited in the skin and tissues, generally together with hæmosiderin. Quincke has described another

process of hæmal pigmentation which he calls siderosis; this must be distinguished from siderosis of the lung, which is produced by inhalation of iron dust, and causes a rusty brown discoloration of the lungs. In Quincke's siderosis there is a deposition of a ferruginous pigment in the liver, spleen, marrow, and often also in the kidneys; this is derived from the red corpuscles which die in the circulating blood, and are then carried by phagocytic cells to the organs mentioned above; from them a yellow hæmosiderin is formed. This process is a physiological one according to Quincke, but under pathological conditions there is increased hæmolysis accompanied by diminished regeneration of red corpuscles, as for instance in pernicious anæmia, when the presence of free iron can easily be demonstrated in the liver, spleen, and bone marrow by means of chemical reagents.

Overproduction of pigment.—(*a*) An excessive amount of brown pigment may appear in situations which normally contain such pigment, *e.g.* the skin, where, for some reason or other, the pigment cells become more active in the elaboration and excretion of pigment. Such overproduction may be physiological, as in the pigmentation of pregnancy; and in freckles (due to exposure to sunlight); it may be congenital, in pigmented moles (nævi pigmentosi). Again, pigment (melanin) may occur in small innocent wart-like or mole-like new growths, or in malignant deposits, such as melanotic sarcoma. Melanin is free from iron, but contains sulphur. In Addison's disease, large areas may be pigmented, but as yet no sound explanation has been offered as to the origin of the pigment and the relation between the diseased suprarenal capsules and the bronzing. Histologically, wandering cells loaded with pigment can always be demonstrated in the skin and even in the lymphatic glands, but seldom in the blood.

(*b*) Under certain pathological conditions, a yellowish-green pigment may appear in morbid growths, more especially in sarcomas (chloromas), and in the so-called xanthoma (xanthelasma), which is occasionally associated with, although it may occur independently of, jaundice. This light pigment is probably a lipochrome.

Pigmentary atrophy.—With advancing age pigment appears in several organs, such as the heart, the liver, the kidneys, the testes, the suprarenal capsules, and the ganglion cells of the central nervous system. The origin of this pigment has not been satisfactorily explained. In the testes and liver it is ferruginous, and may therefore have been derived from the blood, but in the heart it is iron-free. Here it is found in the fibres of the myocardium, collected around the nuclei, obscuring the striation of the cells, and apart from senile changes may appear as the result of a cachexia or marasmus (Addison's disease), and may be so excessive as to produce a yellow or brown discoloration (brown or yellow atrophy) of the heart.

Bile pigmentation.—This is known as icterus or jaundice. Under certain pathological conditions, bile pigment, bilirubin, passes into the circulation by the thoracic duct from the hepatic lymphatics. In this condition the larger bile ducts, or the smaller ducts over a large area of liver tissue, are obstructed, or there is a regurgitation of bile into the smaller canaliculi and the hepatic lymphatics. It is always hepatogenous, that is, the pigment is formed by the liver and in the liver, and not in the blood vessels. The pigment appears in the tissues first as bilirubin, which is apparently identical with hæmatoidin; but if the jaundice persists, the bilirubin is gradually oxidised into biliverdin, the tint of the skin changing from yellow to dark green (black jaundice). Bilirubin absorbed from the liver appears in the urine as such, while hæmatoidin appears as uribilin. The icteric pigmentation is observed in the following tissues:—Skin, conjunctiva, most internal organs, the intima of the larger vessels, the liver cells and the renal epithelium; it is also found in the various serous fluids and in sweat, but not in tears; the brain is always free. If the jaundice is of long standing, the bile canaliculi may be filled with inspissated bile.

The cause of the yellow discoloration in certain forms of anæmia (pernicious anæmia and leukæmia) is not known.

ACUTE INFLAMMATION.

Numerous attempts to give a definition of acute inflammation have from time to time been made, but none of them have been altogether successful. Metchnikoff, studying inflammation chiefly in its relation to bacteria, builds up a theory upon phagocytosis as a foundation. He observes the reactions of the tissue of mammals, frogs, crustaceans, and amœbæ in the presence of micro-organisms, and finds that phagocytosis is the one phenomenon which is seen in all animals in the struggle, and therefrom argues that it is the *primum movens* of inflammation. Such reasoning appears to be unsound mainly because the analogy is incomplete, and it is highly questionable whether it is possible, by going back to such simple animal forms as daphnia and amœba, to analyse such an extremely complex process as inflammation, which, so far as it is known in its true form, occurs only in extremely complex animals. It would be as rational to study mental activity in man and the higher animals by examining an amœba. A process occurring in an animal possessed of highly differentiated nervous and vascular systems, the tissues of which, moreover, are highly complex, cannot be compared with any process observed in an animal the structure of which is very simple, or is represented by a single cell. In defining inflammation, or in describing it, classes of animals homologous in structure, and known to react by what is recognised as inflammation, must be taken.

Adami gives as a definition of inflammation, "*the local attempt at repair after an injury, actual or referred.*" This definition includes phenomena which no histologist would or could regard as inflammatory. The constant renewal of the cuticle would be inflammation. An injury—as, for instance, superficial epithelial lesions—may be repaired without what is generally recognised as inflammation, *i.e.* by regeneration and *direct* repair. Some low forms of animal life are capable of regenerating any part or parts of their body. Regeneration is not the same as repair by inflammation, or *indirect* repair. There is no valid reason for extending the meaning of a term so as to make it answer the requirements of a definition. Inflammation is known by its phenomena and its appearances, and by the changes in the tissues, and unless all these are present there is no justification for speaking of inflammation. A certain process or an attempt at repair in a low form of animal may in some or in many of its phenomena resemble inflammation, and still not be inflammation, which is a complex process and occurs in complex tissues, and whose criterion should be what is known to occur in such tissues, and nothing should be called inflammation that does not agree with observations on animals in which the recognised tissue reactions of inflammation may be met with.

Starting from this point, it will be found that acute inflammation is a reaction of mixed tissues, which occurs only in man and other vascular animals; it is a uniform process, varying, no doubt, in its different types, but in degree only, not in kind; there is a uniformity in the pathogenesis, progress, and morphological attributes of acute inflammatory conditions, which is so striking that nothing should be called inflammation, unless it presents all the essential phenomena which the study of disease in man and other vascular animals has revealed to us. To select phagocytosis, or chemiotaxis, or new formation and repair as essentials, and make them the corner-stones of theories of inflammation, is unjustifiable. Phagocytosis, chemiotaxis, and proliferation are concomitant, or it may be constant, phenomena of acute inflammation, and each one of them may be traced

back from the highest to the lowest form of animal; but surely it is not sound reasoning to evolve the whole process of inflammation from one or two of its phenomena, especially when such phenomena are very primitive protoplasmic properties. Evolution may teach how a property or a character has been acquired; it may indicate something of the phylogenetic origin of an organ or a process; but it nowhere teaches that a complex process in a higher animal type, which can be traced back to some property or function in a lower type, is identical with this property or function. In any appeal to evolution, the thread is often lost and many gaps cannot be filled. Inflammation, as it is known to the human pathologist, *occurs only in certain higher animals in which there is a blood vascular system.* This is the line of demarcation. A vascular animal reacts to a certain stimulus by inflammation, while the same stimulus in an avascular animal may produce some phenomenon which also occurs in inflammation, but of itself is not inflammation.

Analysing the process of inflammation, it is found that (1) without blood vessels there is no inflammation; (2) it is a reaction of vascular connective tissue or of connective tissue, itself perhaps avascular, but in close relation with the vascular system. Inflammation of epithelium does not exist, and true inflammation in really avascular connective tissues, such as cartilage, has not been observed. Inflammation in avascular tissue is said to occur in the cornea, but here an anatomically avascular tissue is in close connection with the circulation by means of the vessels at its periphery and its numerous lymph channels. So slight a lesion of the cornea, in which there is nothing more than a limited destruction and proliferation of the corneal corpuscles, is not and does not end in inflammation; there is simply direct repair; any tissue that has life left after an injury or a loss of substance will at once repair itself or regenerate. As soon as the injury is severe enough to transmit its influence to the vessels around the cornea, all the changes of inflammation become evident. The cornea, therefore, is a connective tissue which is subject to inflammation if the stimulus be adequate; if not, repair occurs without inflammation. An irritant may produce different effects according to its intensity and the method of application; it may produce a slight injury, easily and directly repaired; or a serious injury, followed by immediate death or slow necrosis, or followed by secondary inflammation; or it may produce an acute primary inflammation. Now, because the same irritant is applied to a graduated series of tissue and animals, it is not justifiable to assert that the effect of its action is one and the same process in all cases. No doubt, if the different effects produced are compared, there is a gradual transition from one to the other, but so there is from an innocent to a malignant growth.

A smaller number of vibrations of the mysterious ether results in the subjective sensation of heat, while more rapid vibration of the same ether produces one of light; yet heat is not light. The cornea experiments cannot be used as arguments against the view, originally supported by Cohnheim, that inflammation can occur only in vascular tissues, for as soon as changes which everyone would recognise as inflammation are set up in the vessels around the cornea, the tissue in which they lie has reacted, being, so to speak, drawn into the zone of irritation through the innumerable lymph channels. Inflammation, then, must be regarded as a series of changes, occurring only in vascular or vascularisable connective tissue, or in connective tissue in close connection with the surrounding blood vessels.

Causation.—It is only necessary to mention here that traumatic, chemical, or physical irritants, including foreign bodies and micro-organisms, are capable of reacting on the connective tissue in such a manner as to produce the phenomena and appearances of inflammation. These irritants must possess a certain *relative* intensity, otherwise inflammation may not set in; or if the intensity is too great, necrosis may be the result. The intensity will, of course, vary with the general or local tissue resistance of the individual. In certain diseased conditions, inflammation is readily produced by conditions which are incapable of producing it in health.

·**Processes.**—In acute inflammation, two main processes may be distinguished—(*a*) *exudative*, and (*b*) *proliferative*.

The *exudative processes* are, speaking generally, most evident during the earlier stages, and are concerned especially with the vessels. Fluid and cells may pass through the vessel wall, the fluid being coagulable lymph, which may or may not coagulate, the cells being leucocytes and red corpuscles. The *proliferative processes* are observed in the connective tissue and endothelium, and in the vessels. The fixed and wandering connective tissue cells multiply, and so do the endothelial cells lying in the lymph spaces, and lining the capillary and lymphatic walls. These proliferative changes are best seen in the later stages of acute inflammation. It appears, therefore, that in the earlier stages, if many cells are present in the inflamed area, they are *mainly* leucocytes (*leucocytic infiltration*); while in the later stages the cells are *mostly* derived from the connective tissue or endothelium. The products of proliferation, if repair follows, become converted into fresh connective or fibrous tissue, but when this occurs inflammation is at an end. Speaking generally, it may be said that the more vascular a part is, the more evident are the exudative changes during the earlier stages; and, conversely, the less vascular a part is, the more marked are the proliferative changes during the earlier stages. In any process which is recognised as inflammation, both exudative and proliferative changes always occur.

Acute Inflammation (Connective Tissue Reaction).

EXUDATIVE PROCESSES.		PROLIFERATIVE PROCESSES.	
Vessels.		Connective Tissue.	Vessels and Lymphatics.
Fluid (fibrin).	Cells— (*a*) Leucocytes (leucocytic infiltration). (*b*) Red corpuscles.	(*a*) Fixed cells. (*b*) Wandering cells (small round-cell infiltration). Repair—New connective or fibrous tissue and vessels.	Endothelium.

If the process of acute inflammation in the frog's mesentery be carefully watched, it will be found that dilatation of the small arteries (inflammatory congestion) first makes its appearance, and reaches its height in a few hours. More blood flows into the part, and the veins not participating in the dilatation, the velocity of the blood flow is increased. Gradually, but more slowly, the veins and capillaries dilate, and arteries, capillaries, and veins become turgid, and there is a retardation of the blood flow, the leucocytes arranging themselves along the walls of the veins preparatory to their emigration. In the capillaries,

analogous changes are observed: in some the blood still travels onwards; in others there is merely a flow of plasma-like fluid; while in many the current has ceased altogether (stasis), the capillary being filled with red corpuscles, or sometimes with plugs of white corpuscles (white stasis). *Emigration* (an active process) of leucocytes follows, as in the veins; pseudopodia are sent out through the vessel wall, the whole leucocyte gradually following the extruded part. This is accompanied by a diapedesis of the red corpuscles, at times but slight, at other times very marked, but always present. Amongst and between the capillaries numbers of scattered or aggregated white and red corpuscles are to be seen at this stage. At the same time there is also a transudation of fluid (plasma), sometimes so considerable in amount that the part becomes œdematous (inflammatory œdema).

Exactly similar phenomena are seen in the inflamed mesentery of warm-blooded animals, or in the irritated cornea, the vessels at the corneal margin becoming dilated, this being accompanied by a copious diapedesis and transudation of fluid.

The following is a summary of these conditions:—

Dilatation of arterial vessels (inflammatory congestion and increased velocity).

Dilatation of capillaries and veins (retardation).

With retardation: marginal arrangement of leucocytes.

In the capillaries there may be complete stasis;

Followed by diapedesis of white and red corpuscles.

Transudation (inflammatory œdema).

Although the process of emigration must be regarded as an active one on the part of the white corpuscles, certain co-operating factors must not be lost sight of—(1) Changes in blood current: the quickened stream by centrifugal action drives the corpuscles, which normally travel centrally, against the vessel wall, where they are inclined to adhere on account of their stickiness during the retardation stage. When there is stasis, the marginal distribution of the leucocytes is entirely absent. (2) Increased capillary and venous pressure must to some extent assist diapedesis, especially when (3) the permeability of the delicate vessel wall is increased. That the vessel wall becomes more porous can hardly be questioned. (4) Lastly, the vessel wall must be in a suitable condition to allow the leucocytes to adhere. Before emigration can occur, it appears, therefore, that certain conditions must exist—(a) changes in the blood current, to allow of a marginal distribution of the leucocytes; (b) a suitable state of the vessel wall, without which adhesion cannot take place; (c) amœboid activity of the white corpuscles. Substances which paralyse the amœboid movements of the white corpuscles completely stop diapedesis.

Amœboid leucocytes outside the animal body, whenever they come in contact with the surface of a foreign body, attach themselves and become flattened out; and if the foreign body be porous, having attached themselves, they send out pseudopodia into the pores. It is important to remember that this tactile sensibility of the amœboid leucocyte is a natural property. When the corpuscle comes in contact with the vessel wall, it becomes flattened out, attaches itself, sends a pseudopodium through any pore there may be in the vessel wall, and then creeps into the surrounding connective tissue. If the irritant which causes the inflammation is such that it does not paralyse the protoplasm of the leucocyte, nor prevent the vessel wall from responding to its tactile sensibility of adhesiveness, emigration must take place.

The leucocytes, having passed out of the vessel, begin to wander—migration to the seat of irritation. This is also mainly a pseudopodial act, although it is no doubt favoured by concomitant conditions, such as the exudation currents and the diminished resistance of the tissues. This migration to the seat of irritation is due chiefly to an attraction of the leucocytes by the chemical products of bacterial activity or tissue destruction, *i.e.* chemiotaxis. Certain substances, amongst which are albuminous bodies contained in the bacteria (proteins), and the earlier products of decomposition or necrosis, attract leucocytes. That chemiotaxis, or rather the chemiotactic irritability of the leucocytes, is an important factor in the migration, cannot be questioned; but it does not explain altogether why the cells collect in the inflamed area. In pneumonia, for instance, where a whole consolidated lobe may show all the alveoli full of leucocytes, it is difficult to explain such extensive aggregation on the principle of chemiotaxis. A local and circumscribed attraction may be so brought about, but matters are different when a whole organ is invaded. Moreover, if the aggregation of leucocytes in the inflamed lung were due to chemiotaxis, the blood in the peripheral circulation should be impoverished in white corpuscles. The contrary, however, is the case, for in most cases of pneumonia which run a favourable course there is an extraordinary leucocytosis.

The various forms of leucocytes do not show an equal tendency towards diapedesis or migration. In circulating blood, the following general types of white corpuscles occur, viz.—(1) The lymphocytes; (2) the multinuclear; (3) the large uninuclear; and (4) the coarsely granular eosinophile cells. The small lymphocytes consist of scanty protoplasm, covering a round nucleus, and are indistinguishable from the small cells of lymphoid tissue. They may form up to 30 per cent. of the leucocytes present in human blood. The large uninuclear cells have a round or kidney-shaped nucleus and abundant protoplasm, and are rare in the blood (2 per cent.). The multinuclear or polymorphonuclear cells have a lobed or multipartite nucleus, and their protoplasm is beset with small granules, staining red with eosin. They are abundant in the blood (up to 70 per cent.), and are actively amœboid and phagocytic. The coarsely granular cell shows large and numerous granules, staining deeply with eosin; they are rare in human blood (up to 5 per cent.), are amœboid, but not phagocytic. During the earlier stages of inflammation, when chemiotaxis is said to be most active, the multinuclear (neutrophile) cells leave the vessels in greatest number and migrate to the irritated area, forming the bulk of the pus corpuscles. Sometimes the coarsely granular eosinophile cells also appear in large numbers. This "selective attraction" proves that we must not take the process of chemiotaxis too literally. The cells which migrate to the inflammatory focus are the most plastic and amœboid among the leucocytes, and this demonstrates the close relation which must exist between so-called chemiotaxis, tactile sensibility, and motility. These leucocytes, coming up, draw a cordon around the inflammatory zone, and prevent absorption of the toxic material. Moreover, the cells being phagocytic, they not only destroy the irritant, but assist in clearing away the tissue débris, so preparing the ground for the proliferating connective tissue. At times, however, they have to collect in such enormous numbers that suppuration appears.

A fluid *transudation*, differing but little in composition from ordinary plasma, also leaves the vessels. There is a normal process of lymph transudation, exaggerated as the result of inflammation, varying with the laxity of the tissues, the nature of the irritant and the animal, and inversely as the resistance of the tissues. There is thus a flushing out of the part

and a removal, or at any rate a dilution of the poisonous irritant. This may bring about an increase of the chemiotactic process, for it has been shown by experiments that strong solutions of certain substances may paralyse the tactile sensibility and the motility of the amœboid leucocytes, while when diluted the same solution may produce an attraction for these corpuscles. This fluid may supply the proliferating tissues with nourishment; on the other hand, however, it may prove harmful by impairing nutrition, by the tissues becoming water-logged, by pressure on vital organs, and even on the cells of tissues.

Transudation appears to be due to three chief factors, namely, (1) the increased permeability of the capillary wall; (2) an increased lymph secretion; and (3) a diminished lymph absorption. Some observers deny that there is a true lymph secretion, but regard the process as a mechanical one, *i.e.* a filtration under pressure, and, according to them, instead of increased lymph secretion, increased filtration must be due to raised intracapillary pressure.

The inflammatory exudation consists of plasma or a plasmatic fluid, various enzymes and toxins derived from bacteria, and certain germicidal substances, tissue cells, mucin, leucocytes, fibrin and its precursors, albumoses, and peptones. The exudation may or may not coagulate, according to the presence or absence of the fibrin-forming substance.

Fibrinous inflammation.—Under physiological conditions, plasma will coagulate outside the body, on the addition of fibrin ferment or leucocytes; it may be argued, therefore, that in inflammation, wherever leucocytes are present, fibrin is formed. The absence of coagulation in the case of serous effusion requires explanation. It appears to be due largely to certain inhibitory influences, amongst which may be mentioned— (*a*) integrity of the endothelial or epithelial surface; (*b*) absence of fibrin ferment and leucocytes; (*c*) increased alkalinity; and (*d*) the presence of certain toxic or chemical substances which, in small quantities, are capable of preventing coagulation. Thus, extremely minute quantities of cobra poison will prevent coagulation, and certain bacterial substances or tissue products appear to be possessed of similar powers.

Fibrin generally appears on free surfaces or in enclosed spaces (tonsils, pleura, and pericardium), especially when there is continued rubbing of the surfaces of organs (heart and lungs), or as the result of the action of chemical substances, as in diphtheria and pneumonia. It may be formed either immediately or after some delay, the exudation at first serous, later becoming fibrinous; it may form a true membrane lying on the free surface, as in fibrinous pericarditis, or it may form an interstitial deposit, as in diphtheria, where the fibrin appears between and among the epithelial cells, which undergo a so-called coagulation necrosis.

Serous inflammation.—If the exuded plasma does not coagulate, the inflammation is said to be serous. The fluid poured out, which varies considerably in amount, generally speaking exudes most copiously from a free surface, which may be lined by epithelium, columnar in the nose, larynx, intestine, or uterus, or squamous on the conjunctiva and vagina. A serous inflammation on such free epithelial surfaces is called a catarrh; the exudation then contains much mucus. The effusion may exude from an endothelial surface, such as the pleura or peritoneum. It is possible that coagulation does not occur, because the epithelium or endothelium is intact, or because there are other inhibitory influences which prevent coagulation.

Instead of escaping to a free surface, the exudation may collect in the tissue substance, *e.g.* as in interstitial serous infiltration, in the connective tissue (inflammatory œdema), or between layers of epithelium (vesiculation). An inflammatory œdema is often observed; extensive fibrin formation, as in croupous pneumonia, where, on cutting into the consolidated lung, fluid generally exudes copiously; again, the serous effusion may subsequently coagulate either completely or in part, producing a so-called sero-fibrinous inflammation. In cellulitis and acute septic inflammations, the œdematous infiltration is, as a rule, well marked; indeed, speaking generally, the weaker the local or general resistance of the individual, the more marked is the inflammatory œdema. The fluid which is poured out may be completely absorbed, or it may stagnate, then leading to a chronic or persistent effusion, or to necrosis and gangrene from the impairment of the nutrition of the tissues, which become softened and waterlogged.

Fluid Constituent of Inflammatory Exudation.

Coagulation = fibrinous inflammation.

Absence of Coagulation = serous inflammation = { sero-fibrinous. sero-purulent.

(*a*) Interstitial = diphtheria.

(*b*) Free endothelial surfaces = fibrinous pleurisy.

(*c*) Free epithelial surfaces = membranous tonsillitis, croupous pneumonia.

(*a*) Interstitial = inflammatory œdema, vesicles.

(*b*) Free endothelial surfaces = serous effusion.

(*c*) Free epithelial surfaces = catarrh.

Result { Destruction and removal = resolution. Organisation = induration.

Result { Discharge = catarrh (restitution). Absorption = resolution. Stagnation = chronic effusion. Coagulation = fibrinous or sero-fibrinous inflammation (*q.v.*).

Purulent inflammation.—When emigration and aggregation of leucocytes are excessive, and there is no coagulation, the exudation becomes converted into pus. Microscopically, the so-called laudable pus of the older writers is a thick, viscid, light yellow, or yellowish fluid, with a faintly sweetish, sickly odour; on standing, it separates into two portions, a serous element, the liquor puris, and a whitish sediment, the pus corpuscles. Although pus consists of inflammatory plasma and leucocytes, it does not coagulate, so that there must have been influences or substances at work which, during the process of pus formation, inhibited coagulation. Microscopically, the most important constituents of pus are the pus corpuscles, which are mostly of leucocytic origin. In fibrinous inflammation, *e.g.* in pneumonia, where the number of white corpuscles present may be as great as in pus, the process cannot be compared to a suppuration, as has been done by some observers. The leucocytes, which constitute the pus corpuscles, are mostly actively amœboid, and are usually of the so-called polymorpho-nuclear or neutrophile variety; sometimes, however, the number of coarsely granular eosinophile cells present is striking. Young connective tissue cells are also often found amongst the pus corpuscles; many of the cells are degenerated or dead, but many are still amœboid, well preserved, and phagocytic, as may be seen on placing fresh pus on the warm stage of a microscope.

Pathogenesis of suppuration.—In most cases micro-organisms are present, and it must be concluded that pus is usually of bacterial origin. It is possible, however, by means of nitrate of silver, turpentine, castor-oil, perchloride of mercury, and other chemical substances, to produce a suppuration without micro-organisms appearing (sterile suppuration). Similarly, continued irritation, *e.g.* the presence of metal in the anterior chamber of the eye and the products of necrosis, may call forth a suppurative process. Chemical irritation, therefore, may be a cause of suppuration. Buchner has shown that castor-oil causes a necrosis of the tissues, and that the products of this necrosis have a positive chemiotactic action, *i.e.* they attract leucocytes, and that suppuration is thus set up.

Most cases, however, are of bacterial origin, a fact which the surgeon especially should remember ; and certain micrococci are so constantly found in pus, that they are regarded as pus-producing or pyogenetic organisms. The commonest forms are the following:—(1) Staphylococci : (*a*) *Staphylococcus pyogenes aureus ;* (*b*) *Staphylococcus pyogenes albus ;* (*c*) *Staphylococcus pyogenes citreus.* (2) Streptococci : (*a*) *Streptococcus pyogenes ;* (*b*) *Streptococcus erysipelatis ;* (*c*) *Pneumococcus.* Each variety may occur alone, but mixed purulent infections are frequently met with. Other microbes may produce a suppuration, *e.g.* the bacillus of typhoid fever, the gonococcus and the bacillus of tuberculosis ; but they are so markedly specific in their action, that they are not included among the pyogenetic organisms. How do these germs produce suppuration ? Buchner has clearly shown that they act by *chemical irritation,* for the dead bodies or the protoplasmic substances (proteins) of the bacteria produce suppuration as effectively as, or even better than, the living organisms. The chemical irritant is extremely chemiotactic, and stimulates the leucocytes to emigrate and to wander to the seat of lesion. There appear to be two necessary conditions, without which there can be no pus—(1) chemiotaxis and aggregation of leucocytes, and (2) inhibition of coagulation. A third factor is histolysis or tissue destruction. Under the influence of pus formation, the tissues are dissolved and disintegrated, and, according to the law of repair, they react against this dissolution by proliferation and an attempt to form new cells. This may be observed at the margins of any suppurating focus, and it is for this reason that connective tissue cells are so frequently found in pus.

The fluid constituent of pus is serum devoid of fibrinogen, but containing albumoses and peptones, toxines of bacterial origin, and various products of degeneration. The albumoses and peptones are in part due to the digestive or proteolytic action of the micro-organisms concerned, and partly to a similar action on the part of the pus corpuscles themselves ; indeed, it is probable that the histolysis depends on this proteolytic property of pus. Pus forms a bad soil for the growth of bacteria ; it has, indeed, a distinctly germicidal action, and long pent up in the body becomes sterile, the pyococci being gradually destroyed. The chief physiological properties of pus, therefore, are the following:—It is (1) bactericidal, (2) histolytic, (3) contains phagocytic elements, and (4) is a strong solvent, for Leber has shown that it is capable of dissolving such metals as platinum and copper, which require strong acids for their solution. There can be no doubt that suppuration must frequently be a useful issue of the inflammatory process, assisting in the destruction of the irritant, and stimulating the tissues to react by proliferation. It is often, however, a source of danger, leading to the destruction of the tissues, laying open the vessels, and thus offering openings for serious complications, such as septicæmia and pyæmia.

It would be erroneous to suppose that pyogenetic microbes have an absolutely specific action, and are capable of producing suppuration only. Suppuration is merely the outward expression of certain inflammatory processes, and it is not even the most serious phase or variety of inflammation. As a matter of fact, it found that the same species of organisms may produce a slight local inflammation or an extensive spreading inflammation, a small local suppuration or a large acute abscess, an erysipelas or a cellulitis, a pneumonia, a septicæmia, an infective endocarditis, or a pyæmia. Thus a small acne pustule may contain one or more varieties of pyococci. It may grow into a boil, the latter into a carbuncle, which, again, may be followed by septicæmia or pyæmia. The pneumococcus may be found in pneumonia, in suppurative otitis media, in angina Ludovici, in infective endocarditis, peritonitis, and pleurisy. Almost all vegetable micro-organisms possess the faculty of producing an inflammation, and those which are most frequently found in primary inflammatory processes are called pyogenetic, but whether they produce a benign form of inflammation, or a suppuration, an œdematous or a necrotic inflammatory lesion, will depend chiefly on the virulence of the bacteria, and the local conditions, the local or general resistance, on the quantity of bacteria introduced, and on the continuance of the supply of micro-organisms, *i.e.* whether there is a single or a continued invasion of micro-organisms. Under favourable conditions, *i.e.* if the virulence of the bacteria be reduced, or the resistance exalted, an innocent local inflammation may ensue; as the virulence increases, or as the resistance decreases, suppuration makes its appearance; and if the virulence is excessive, and the resistance slight, an œdematous, necrotic, or gangrenous inflammation is produced. Septicæmia appears when the organisms enter the circulation and multiply in the blood. It is of the utmost importance to realise that suppuration is not a specific process: it is a clinical term for changes which can be recognised by the unaided eye.

The character of the pus varies considerably. (1) Thus it may be thick, creamy, light yellowish, or greenish in colour, possessing a characteristic faint odour (laudable pus, which is oftenest associated with staphylococci). (2) It may be serous and thin, when the streptococcus is also not uncommon. (3) Its colour may be blue or green, due to the presence of the *B. pyocyaneus.* (4) In typhoid suppuration the pus is generally thick and reddish in colour, (5) while gangrenous pus is usually associated with a mixture of organisms (mixed infection). It must not be imagined, however, that it is possible to recognise the bacterial infection from the appearance or character of the pus, which can only be gauged by means of the cultivation tube, all the more since usually two or more species of pyogenetic organisms occur together.

A suppurative process may be either primary or secondary, *i.e.* it may be the only lesion present, or it may appear in the course of or after the defervescence of an infective fever. Thus an abscess may be due to some injury followed by infection (primary suppuration); another may occur during or after an attack of enteric fever (secondary suppuration). In the latter case the suppuration may be due to the organisms which caused the fever, *B. typhosus* (homologous infection), or it may be due to an altogether different organism, a streptococcus or a staphylococcus (heterologous infection).

Anatomically, suppuration may be superficial, or interstitial; that is, pus may either be discharged from a free surface or it may collect in the deep tissues. When the process is superficial, it may appear (*a*) as a result of inflammation of a mucous membrane,—pyorrhœa, or (*b*) of a serous membrane,—empyema. Pyorrhœa may or may not be accompanied by superficial ulceration. The term *empyema* is now generally applied to

suppuration of the pleura. In interstitial suppuration the pus may remain (1) localised, forming an *abscess* which may or may not be surrounded by a capsule, or (2) it may infiltrate the connective tissues. The *purulent infiltration*, by destroying the tissues bathed by the pus, may become converted into an abscess. If the pus infiltrates the epidermis, the result is a *pustule*, which in reality is an epidermal abscess.

Suppuration.

1. *Superficial*—	2. *Interstitial* { Connective tissue = abscess ± capsule.
(a) Mucous membrane = pyorrhœa ± ulceration.	(a) Localised: Epidermis = pustule.
(b) Serous membrane = empyema.	(b) Infiltrating: may become an abscess.

The pus which has been formed (if small in amount) may be reabsorbed on cessation of the irritation of inflammation. This is effected in part by phagocytosis, in part by the proliferation of the endothelial and connective tissue cells. Proliferative changes there always must be, because during suppuration there is always histolysis, and the destroyed tissue must be replaced by fibrous tissue (*indirect repair*). The pus may remain behind, and result in the formation of a chronic abscess, which may have a distinct fibrous capsule, and on cessation or abatement of the inflammation the capsule becomes smooth, and forms the so-called *pyogenic membrane* of older writers. In most chronic abscesses inflammation and suppuration continue, micro-organisms flourish in the pus, and they, with their poisons, act as irritants. In some, however, all inflammation ceases, the micro-organisms perish, symptoms due to pent-up pus often being entirely absent (*cold abscess*). On the other hand, the unabsorbed pus may become *curdy and inspissated*, caseous, or even calcareous or cretaceous, as the result of a deposition of calcium salts; calcification is always preceded by inspissation or caseation.

Pus.

Reabsorption.	Retention.	
	Liquid—	*Inspissated*—
	(a) Chronic abscess.	(a) Curdy.
	(b) Cold abscess.	(b) Caseous.
		(c) Calcareous.

Hæmorrhagic exudation.—Under certain conditions the diapedesis of red corpuscles may be excessive, the exudation becoming hæmorrhagic. In such cases leucocytes are generally scarce; there is a *blood-stained serous exudation*, but occasionally the red corpuscles are mixed with the leucocytes and round cells, which have been collected in large numbers at the inflammatory centre—*blood-stained purulent exudation*.

The excessive diapedesis of the red corpuscles is due mainly to the activity of the irritant, or to lowering of the resisting powers of the tissues. Virulent infections, such as smallpox, malignant pustules, and acute necrosis, are frequently accompanied by hæmorrhagic exudation; whilst in a debilitated subject, suffering from renal disease, inflammations readily become hæmorrhagic. In gangrene,

where the toxines are powerful and absorbed in large quantities, the vessels are injured, and hæmorrhages, due to direct rupture, or indirectly to diapedesis, are common. Again, in the early stages of acute inflammation, hæmorrhagic exudations are common; in the first stages of acute nephritis the urine is often red from admixture of blood (nephritis hæmorrhagica). A mechanical injury may cause vascular lesions, gross or minute, by which the blood finds an outlet and mixes with the inflammatory exudation; this, however, is a true hæmorrhage, and is very different from hæmorrhagic inflammation, where the blood transudes by a process of diapedesis; the former is a hæmorrhage *per rhexin*, the latter a hæmorrhage *per diapedesin*. Again, inflammation may occur in a part the venous circulation of which is laboured and obstructed, *i.e.* in an engorged area. Here there is considerable slowing of the blood stream, marked fulness of the venous channels, and grave disturbance of nutrition.

Hæmorrhagic Inflammation.

(1) *Direct hæmorrhage* (per rhexin)	(2) *Indirect hæmorrhage* (per diapedesin)
= lesion of vessel wall, gross or minute.	(a) Intense irritation. (b) Early stages of acute inflammation. (c) Venous engorgement. (d) Loss of local or general tissue resistance.

The proliferative changes of acute inflammation are best seen when the exudative changes are clearing away, but it is erroneous to imagine that in point of time they follow the exudative phenomena. They may be observed at the margins of the affected area, even at the earliest stage of inflammation, but they become more evident with the disappearance of the leucocytes; the veil is lifted, and a clear view is obtained, and they persist, passing on imperceptibly to play a part in the stages of repair. Repair is not necessarily a termination of inflammation, but proliferative changes are always present. An injured tissue which has any life left, is always ready to react by repair; if there is loss of substance, the living cells multiply and proliferate; if there is no loss of substance and no necrosis, but merely damage to the cell, the cell itself may recover. There are, therefore, two processes by which an injury is made good—(a) recovery, (b) repair by proliferation. The latter may or may not be accompanied or preceded by inflammation. Thus an injury to a tissue may not be sufficient to cause proliferation of the connective tissue; repair is then direct, the cells proliferating and producing homologous tissue; if, however, it be sufficient to rouse the connective tissue to inflammatory reaction, repair is indirect: matter has to be cleared away, the resulting gap has to be filled up, and this can only be done by fibrous tissue, *i.e.* by heterologous tissue. It is the nature of things that reparative changes should appear in inflammation, the remaining living tissue tends to repair an injury; that is a postulate of pathology. The least injured cells recover, the more injured ones die, but their places are supplied by a new progeny. Since in inflammation there is always some necrosis, therefore some proliferation, proliferative changes are necessarily present in inflammation. These changes are observed—(1) in the connective tissue cells, (2) in the endothelial cells of the lymph spaces and capillaries. The connective tissue cells enlarge; their nuclei become swollen, round, or oval, and karyokinesis (mitosis) is active; this is certain evidence of

proliferation. The leucocytic infiltration may be so considerable as to hide the proliferative phenomena altogether, but as soon as the leucocytic infiltration clears up, which it always does as the inflammation subsides, what has taken place may be clearly seen. There are many large protoplasmic cells, rich in cell substance, and with nuclei which stain but faintly, or are rich in chromatin and resemble epithelial cells, and are therefore usually spoken of as epithelioid cells. Others are more fusiform in shape, with long darkly staining nuclei; these gradually become spindle-shaped. It is generally believed that the spindle cells are merely a later stage of the epithelioid cells, *i.e.* that both are derived from the connective tissue cells, although some observers maintain that the spindle cells are derived from the fixed connective tissue cells, and the epithelioid cells from the endothelium. At this period, when the leucocytic infiltration has disappeared and the cells begin to proliferate, numbers of small uninuclear round cells appear, which possess a large round nucleus and resemble lymph corpuscles (lymphocytes). These small cells are collected in irregular groups or in distinct masses, which may be compared to adenoid or lymphoid collections, and they constitute the small round-cell infiltration (lymphocytic infiltration). These small cells appear to be derived from rapidly proliferating connective tissue cells, from the endothelium of the lymphatic spaces, and from the lymphocytes which are always present in the connective tissue; but many of them may have been attracted by so-called "chemiotactic" influences. The free connective tissue cells, the lymphocytes, and the endothelium of the lymph spaces are all migrating, and may therefore be attracted to the seat of irritation.

The normal connective tissue possesses (a) fixed cells and (b) wandering cells; but while only the latter are free and under the spell of chemiotaxis normally during inflammation, the fixed cells, as they divide and proliferate, may become free and wandering. Migrating to the seat of inflammation, they are at first mixed up with the emigrated leucocytes in the exudation, and assist the latter in clearing away the irritant, foreign and dead matter, hæmorrhages and fibrin; they also take up the remains of dead leucocytes, which have done their share of the work, and thus complete the cleansing process. When everything is cleared away, they either fall into their proper places, or they undergo further changes and form vascular cicatricial tissue. A croupous pneumonia, for instance, may clear up, the leucocytes disappearing, being in part discharged with the expectoration, in part taken up by the connective tissue cells and the endothelium; these cells may then simply resume the places they ought to occupy, so that the result is a complete resolution without secondary thickening, or they may form vascular connective tissue, which gradually becomes fibrous and leads to a chronic induration of the lung. Resolution then corresponds to homologous repair, induration to heterologous repair (cicatrisation). When cicatrisation occurs, the proliferated cells become spindle-shaped, arrange themselves in strands along the vessels, more and more interstitial substance appears between the cells, which have become still more fusiform, and are now called fibroblasts. The latter become gradually less protoplasmic, while the interstitial substance increases, and gradually typical fibrous tissue is formed, which in time becomes harder and less vascular.

It is during the earlier stages of repair that phagocytosis is best seen. The connective tissue cells take up the dead tissues, leucocytes, foreign bodies, etc., following the example set them by the leucocytes. If the material to be removed is copious or firm, giant cells—multinucleated cells with numerous nuclei, and often provided with branched processes—appear. They are both phagocytic and histolytic, devouring and dissolving the substances with which they come in contact.

During the process of heterologous repair new vessels appear. These are

formed from the original vessels, which throw out endothelial buds into the inflammatory area occupied by the proliferated cells, *i.e.* by the small round cells forming the lymphocytic infiltration.   At a given point the endothelial cells divide and multiply, until a solid endothelial protrusion is formed.   This becomes hollowed out, the blood extending into it from the old vessel.   These newly formed vessels are surrounded by numerous small round cells, amongst which are spindle cells, epithelioid cells, and large protoplasmic cells, and, under the above-mentioned conditions, giant cells.   Such vascularised proliferating cellular tissue constitutes the so-called granulation tissue of the surgeon, which gradually becomes converted into cicatricial tissue.   As the cicatricial tissue becomes more fibrous, the vessels gradually disappear, and a hard, dense, white or glistening fibrous tissue remains.

It should be remembered that as soon as resolution or repair sets in, inflammation is at an end, and further that cicatrisation may take place without the occurrence of preceding inflammation.

Abscess and ulceration.—Of the clinical results of inflammation, abscesses and ulcers require special mention.   Abscess is a local collection of retained or pent-up pus, buried in the depth of the tissues. If the early leucocytic infiltration is excessive, the inflammatory exudation assumes the characters of pus, being whitish in colour, when enough pus is formed to be detected with the unaided eye.   The newly formed pus, acting destructively on the surrounding tissue, assists the original irritant.   The inflammation thus progresses, more leucocytes are attracted, and the proliferating tissue and endothelial cells are compelled to withdraw, being destroyed by the spreading suppuration.   A growing collection of pus is thus pent up in the tissues, and an acute abscess is the result.

Should the process last for some time, or the irritant be abated, the proliferating cells may gain the upper hand, and the granulation tissue, which may eventually become changed into fibrous tissue, is formed: the collection of pus is thus enclosed by a fibrous membrane,—a pyogenetic membrane.   There may be all gradations of structure in this wall from a fibrous membrane to soft granulation tissue.   In the latter case the granulations continue to discharge pus, and the abscess grows; where a typical fibrous membrane is present, pus formation has ceased.

An ulcer, when acute, is merely an inflamed and suppurating surface of the skin or mucous membrane, accompanied by, or resulting from, necrosis.   Necrosis, whether caused by inflammation or by any other cause, implies loss of substance, a loss that has to be made good.   Inflammation follows upon necrosis, if it did not exist before, and as recovery takes place gradually, the proliferative changes become more and more apparent, the necrotic tissue being dissolved and absorbed, and granulation tissue developed.   So long as the slough and the irritant cause remain, the granulation will discharge pus, but gradually, as the slough is cast off, the discharge of pus ceases, the granulations become fibrous tissue, and the cutaneous or mucous surface is restored.   An ulcer may therefore be compared to an open abscess; both when of some standing being lined by granulations, and when acute being marked off by typical inflammatory tissue.   The necrosed tissue may show itself either as a coherent piece of dead tissue, a slough, or as a friable structureless mass.

Septicæmia and pyæmia.—Of the complications of inflammation the most interesting, if not the most important perhaps, are septicæmia and secondary infections.   The commonest causes of inflammation, as already seen, are micro-organisms, and the complications here considered are

closely bound up with the fate of these micro-organisms in the tissues. Whether one of the pyococci, or a specific bacillus such as the bacillus of typhoid fever, diphtheria, or tuberculosis, caused the initial inflammatory lesion, their future is governed by the most diverse circumstances.

1. They may remain localised at the seat of infection, where they produce simple inflammation, or its various modifications. Here they may soon perish, the phenomena of inflammation coming to an end, or they may be pent up or retained, together with some of the inflammatory products, and acting as a continual irritant, a chronic suppuration results. This leads to chronic abscess and chronic ulceration. The micro-organisms continually irritate the imperfectly formed, immature, and delicate, vascular, connective tissue, and the inflammatory exudation, generally in the form of pus, persists. The micro-organisms, growing quietly and undisturbed, produce their poisons or toxines, which being absorbed lead to chronic intoxication (*toxæmia*), the effect of which may show itself as fever of a remittent, intermittent, or hectic type. Thus, where there are abscesses hidden in the tissues, as for instance in the lung or liver, the thermometer often reveals the existence of a suppurative fever; the same type of fever occurs with typhoid ulcers and with tuberculous lesions.

2. On the other hand, the organisms may not remain localised, but may be carried away from the primary seat of lesion. The paths by which they travel may be (*a*) either the lymphatics, (*b*) or the blood vessels. The pathogenetic organisms being mostly parasitic, *i.e.* capable of thriving in or on living tissues, may travel along the lymph channels into the surrounding tissues, and form fresh foci of inflammation or suppuration at some distance from the primary area (secondary infections). Thus, in croupous pneumonia, the pneumococcus may be carried into the pleura, the pericardium, or the peritoneum, by the lymph channels, and there produce inflammatory changes. Again, the lymphatics may transfer them to the nearest lymphatic glands, which in turn become inflamed or form fresh foci of infection. Thus, in typhoid fever, bacilli are carried to the mesenteric glands, or, again, streptococci, with or without diphtheria bacilli, find their way into the cervical or bronchial glands during an attack of diphtheria, or suppurating glands may appear in the groin as a sequela to an ulcer in the foot. In such cases the symptoms may be those of a serious and severe intoxication, the foci whence poison may be absorbed being or becoming numerous and extensive. An infected lymphatic gland may become the source of a general infection, if a communication is established between it and the blood circulation through the thoracic duct. Thus Weigert has demonstrated that in acute miliary tuberculosis the thoracic duct is frequently tuberculous, and by this path the tubercle bacilli reach the systemic circulation. They may then be carried away as bacterial emboli into distant parts, or they may multiply in the circulation, producing a hæmic infection. It is a curious fact that most morbid anatomists are satisfied in cases of acute miliary tuberculosis when they are able to demonstrate a caseous focus somewhere in the body, but they do not attempt to find the actual point of entrance into the systemic circulation.

The diffusion of the organisms which are responsible for the primary infection may, however, be brought about by the blood vessels. Here two methods of dissemination must be distinguished.

(1) The venous channels being eroded or laid open during and by the process of histolysis, a few microbes may find an entrance into the blood stream, and then one of several things may happen.

(*a*) The blood may possess sufficiently strong bactericidal power to cope with and destroy the few organisms which have found their way into the vessel. This is the most fortunate termination of what might be a serious accident, for no evil will come of this hæmic invasion ; (*b*) the micro-organisms may escape the deadly action of the blood, and, without multiplying in the circulation, they may be carried away as emboli through the heart into the systemic, pulmonary, or portal circulation, till arrested at some narrow point. Here, if suitable conditions exist, they will gain a footing and form a fresh focus of inflammation or infection, *i.e.* a *metastatic* or *secondary focus*, due to the arrest of a bacterial embolus, is formed. If conditions at the point of arrest are not suitable, the micro-organisms may perish, but they may remain latent, and survive, inoffensive and harmless, until such conditions arise as will awaken them into dangerous activity. Thus, in typhoid fever, organisms are almost constantly found after death in the bone marrow ; there they have been carried from the seat of ulceration to the blood and through the heart. Here they enjoy an existence of inactivity, till perhaps an injury to the bone or a general tissue depression resuscitates them into aggressive virulence. (*c*) The micro-organisms may find the blood so impoverished that its bactericidal power has vanished, and they may then multiply in the circulation, and produce a general hæmic infection, — a septicæmia. In septicæmia, micro-organisms are found in the circulation, where they multiply and thrive, and produce their poisons. Nothing should or must be called septicæmia, unless there be general hæmic infection (demonstrated by cultivation), whatever may be the clinical prejudice. Any inflammatory infection may end in this untoward manner, *e.g.* pneumonia, typhoid fever, sore throats, acute necrosis, erysipelas, cellulitis. When symptoms point to serious complications, a thorough examination of the blood for hæmic infection renders it possible to pronounce upon a most serious prognosis, and, in these days of serum therapeutics, to adopt appropriate treatment.

A general hæmic infection may, however, start in a roundabout way. A bacterial embolus may enter a venous channel, and may find its resting place on one of the cardiac valves, where, should the organisms find the conditions necessary for their growth, an infective endocarditis must result. From the infected valve micro-organisms may be poured into the circulation, till the hæmic infection is complete. Again, a metastatic focus, produced in the following manner, may become the starting-point of a hæmic infection, or an infective endocarditis which generally implies hæmic infection.

Infected fibrinous or tissue emboli may take the place of simple bacterial emboli. The veins at the seat of inflammation become plugged with fibrin, the thrombus is invaded by micro-organisms, and thus become infected. From this infected and contaminated mass, fragments may be carried off by the blood current to the right side of the heart, where they may become attached to the tricuspid valve and form the starting-point of an infective endocarditis. If not arrested there, the embolus is carried into the lung, and may become lodged in some arterial branch, producing an infected infarct. The embolus may, however, be carried right through the lung into the left ventricle, and thence may enter the aorta and the systemic circulation, or it may become fixed on the mitral valve. It is natural that, when an infective endocarditis appears, micro-organisms will readily find their way into the general circulation, and from the diseased valve bacterial or infected fibrinous emboli may enter the circulation and produce fresh metastatic foci or

general hæmic infection. It stands to reason that the presence of metastatic abscesses, clinically called pyæmia, does not of necessity imply that micro-organisms are found in the blood, that is, that there is septicæmia. (2) The micro-organisms may be carried away from the seat of lesion by the arterial channels. A small artery, for instance, although the elastic coat is very resistant against infection of any kind, may be attacked and pierced by the micro-organisms, which are then carried away as bacterial emboli towards and into the capillary area.

In septicæmia an inflamed area becomes invaded by saprophytic and putrefactive organisms. These latter thrive on dead or dying tissues, but cannot grow on healthy or living tissues; sapræmia, therefore, commonly accompanies gangrenous or ulcerated lesions; and in childbed, with which there is much necrosis, the microbes produce their toxines, which are absorbed, and serious symptoms of sapræmia may result. When the necrotic area is removed, the bacteria, which cannot grow in living tissues, disappear; the symptoms of sapræmia subside, and the patient usually makes a speedy recovery. Septicæmia, or hæmic infection, can obviously never be produced by true saprophytes. In the following table are tabulated the various paths of dissemination :—

Infection of an ulcerating or necrotic area by saprophytic organisms, accompanied by general intoxication, with their products.	*Sapræmia.*	Recovery after radical removal, so long as the amount of toxines absorbed are sublethal.
Infection of an inflammatory area by parasitic organisms, accompanied by general intoxication, with their products.	*Septic Infection and Intoxication.*	Lymphatic infection, direct retention (cellulitis); glands (buboes), septicæmia; thoracic duct, multiple emboli. Hæmic infection = septicæmia. Bacterial emboli { Metastatic infection (pyæmia); hæmic infection. Infected fibrinous emboli { Metastatic infection (pyæmia).

To give a few examples. In suppurative otitis media, the pyococcal infection may remain localised or may spread to the brain, leading to a temporo-sphenoidal or cerebellar abscess, or it may spread into the lateral sinus or into the jugular vein, and thence into the right side of the heart, producing an infective endocarditis and general hæmic infection (septicæmia). This may be accompanied, or followed, by multiple embolism, with metastatic deposits in the lungs, spleen, and elsewhere (pyæmia).

In a case of typhoid fever with ulceration in the intestines, and in the ulcers besides the typhoid bacilli there are streptococci which may be swept away by the blood stream, and deposited in the bone marrow, where, under suitable conditions, they may produce a secondary lesion, an osteomyelitis. On the other hand, entering the blood stream they may multiply, and set up a general hæmic infection or a septicæmia, in some rare cases with infective endocarditis, and secondary deposits in the body (pyæmia). Even the typhoid bacilli themselves

may be carried away by the blood stream, whence they may be thrown out in the urine, or they may be stored up in the bone marrow. There, under provocation, they may produce a typhoidal osteomyelitis. Rarely they may multiply in the blood, and give rise to a true typhoidal septicæmia. In croupous pneumonia similar processes may be noted; the pneumococci may extend locally into the pleura or pericardium, the effect of such extension being a pleurisy or pericarditis; again, in endocarditis, a few cocci may be carried away by the blood into the meninges without the blood itself becoming infected; or a hæmic infection may occur directly from the lungs or indirectly through the endocarditis. In the latter case pneumococci will be found in the blood, and there may be multiple metastatic foci of a suppurative nature.

As regards the *anatomical distribution of the metastatic or pyæmic foci*, even a casual observer will notice that when the primary focus is in the area of the pulmonary or the systemic circulation the liver generally escapes the metastatic dissemination. If a pulmonary infective lesion is followed by pyæmia, metastatic deposits occur mainly in the systemic, but frequently also in the pulmonary vascular area; if a systemic infective lesion is followed by pyæmia, metastatic deposits are found mainly in the pulmonary, but frequently also in the systemic vascular area. Pyæmic deposit in the liver (portal pyæmia) is often observed in the post-mortem room; the primary focus in such cases is always in the portal area. An embolus is carried up by a venous radicle of the large or small intestine, and, entering the portal vein, is finally arrested in the terminal distribution of this vein. Such a primary portal focus, however, may also produce a metastatic deposit in either the systemic or the pulmonary vascular area. A minute bacterial embolus may pass through the entire portal zone into the vena cava, and thence into the right side of the heart, to be deposited in the lungs or in the systemic peripheral area. Similarly, an embolus may be carried through the systemic circulation into the liver.

The following table will serve to summarise these considerations :—

Primary Focus.	Metastatic Deposits.
Pulmonary area	{ Systemic area. { (Pulmonary area.)
Systemic area	{ Pulmonary area. { (Systemic area.)
Portal area	{ Portal area. { (Pulmonary area.) { (Systemic area.)

General hæmic infection may owe its origin to a primary focus situated anywhere, whether in the pulmonary, systemic, or portal area; and when a general septicæmia has developed, metastatic deposits may appear in any region of the blood vascular system, because the arteries may carry the organisms indiscriminately over the body.

Septicæmia may occur without any recognisable local infection, *i.e.* idiopathic or, better, cryptogenetic septicæmia. No primary focus is found, yet pathogenetic bacteria are found in the blood and organs. These organisms must have obtained access to the blood from the respiratory or alimentary tract or from the skin, parts always in contact with bacteria. A slight loss of substance, such as an abrasion, is sufficient to open up the way, whilst it must also be remembered that the adenoid structures of mucous membranes are, even in the normal state, but scantily and incompletely covered by epithelium. A minute superficial lesion may easily

escape detection, when methods are used which, if the size of a micro-organism be considered, are very coarse indeed.

CHRONIC INFLAMMATION.

The term chronic inflammation covers processes which are essentially different, namely, chronic fibrous changes, chronic catarrhal conditions, and chronic suppuration. When pus is continually discharged, whether it be from an open ulcer or a closed abscess, or a large area healing by so-called second or third intention, there is always a granulating surface. In such processes, which is chronic, the discharge or the inflammation? Undoubtedly the purulent discharge. Granulations are made up of extremely delicate, vascular, undeveloped connective tissue, which is easily irritated, becomes inflamed and suppurates, and as new granulations spring up, they again become inflamed and suppurate; or if the irritation, inflammation, and suppuration persist, more of the surrounding healthy tissue is attacked, and it in turn becomes inflamed and suppurates. Hence the irritation, acting ever on fresh tissues, sets up an ever repeated process of acute inflammation, affecting always different parts, or destroying one part and then attacking a fresh part, *i.e.* there is chronic irritation continually provoking inflammation, and producing a lasting suppuration of an ever-changing surface. The suppuration of these numberless foci of inflammation amounts to chronic suppuration; it is only observed where there is granulation tissue. From the pathological point of view this is not chronic inflammation, but chronic irritation of such intensity as to produce suppurative inflammation of the delicate granulation tissue as it appears, or to destroy the superficial granulations, and to act on the freshly exposed tissues. The irritation is the constant quantity, but the suppurating surface changes. Removal of the irritant under suitable conditions will at once allow the granulations to advance to cicatrisation. In this country, therefore, continued suppuration, or a continued ulceration, or a hidden and lasting abscess, are not as a rule regarded as chronic inflammation.

Histologically, the various forms of so-called chronic inflammatory processes may be classified under several headings:—(1) In some there is *hyperplasia* or proliferation of the connective tissue; or, if a mucous membrane be affected, a hyperplasia both of the epithelium and under-lying tissues, in which sometimes the glands also share; (2) in others, so-called *catarrhal conditions,* when the lesion occurs in a secreting tissue; (3) or an *interstitial fibrous change;* and (4), finally, in others a *complete replacement* of the primary elements by fibrous tissue.

In chronic inflammation of the vocal cords, there may be noticed chiefly—(*a*) proliferation and hyperplasia of the subepithelial connective tissue, *i.e.* fibrous hyperplasia, or, in more modern language, fibrosis; (*b*) proliferation and hyperplasia of the epithelium itself, which frequently becomes horny; and (*c*) proliferation of the capillaries and vascular elements. The proliferation may be so complete and uniform as to lead to a papillomatous growth or a pachydermia.

Compare and contrast with this chronic cervical catarrh, in which similarly there are—(*a*) proliferation and hyperplasia of the subepithelial connective tissue; (*b*) proliferation and hyperplasia of the secreting epithelium itself, leading to dilated and elongated, or even cystic follicles, lined often by several layers of columnar epithelium; and (*c*) proliferation of the capillaries and smaller vessels. Here the proliferation may be so complete and uniform as to lead to a

beautifully papillomatous surface.   The proliferated epithelium retains its secretory activity, hence the catarrhal flow.   This is the only apparent difference between this affection and the laryngeal form; the squamous epithelium is not secretory in the ordinary sense of the term, and there is no catarrhal flow.   In one case the catarrhal flow, in the other increased formation of horny substance, mark the increased functional activity.   In point of principle, there is no difference between these two processes, which at first sight appear to be distinct; and therefore to the three factors mentioned, namely, hyperplasia of the connective tissue, hyperplasia of the epithelium, and slowly increasing vascularity, a fourth must be added, namely, increased functional activity.   These changes are frequently, if not commonly, found in so-called chronic inflammation of mucous, muco-cutaneous, or cutaneous surfaces.   But in the fibrous changes only is "fibrosis" an essential attribute of chronic inflammation.

In some cases, in place of hyperplasia, there is atrophy of the mucosa, as in atrophic rhinitis or gastritis.   During certain stages, at least, firm fibrous tissue is formed, contracting from the surface, and, so to speak, smothering the glands.   These for a long time remain functionally very active—*teste* the fœtid secretion of ozæna, or the cystic dilatation of the glands in atrophic gastritis.   Instead of a hyperplasia, there is an induration of the connective tissue, without proliferation of the surface epithelium or the capillaries.   This induration could not have occurred without previous proliferation, the newly-formed fibrous tissue becoming condensed as soon as it is formed; it required a proliferative stimulus for induration or sclerosis to ensue.

Why do some newly formed fibrous tissues contract and others go on increasing?   A scar will generally condense into hard fibrous tissue, but occasionally it becomes cheloid.   Grawitz lays it down that the connective tissue "having once awakened," there is no limit, necessarily, to the energy of its waking hours; it may go on unchecked, in a condition of morbid insomnia, but it usually stops at a certain point, where it may cease, or the tissue may become condensed, hard, or indurated.   It must further be remembered that atrophy and polypoid hypertrophy (in the stomach, for instance) may occur together.   Again, epithelial proliferation is frequently present in atrophic "inflammations"; in ozæna the stinking mucosa may be lined by several layers of squamous epithelium, the product of a proliferative metaplasia, and papillomatous cysts occur in atrophic gastritis.   So that even in these conditions three of the four above-mentioned factors are present, although in modified form, namely—(1) induration of the subepithelial connective tissue; (2) partial or complete proliferation of the epithelium; and (3) increased, though altered, functional activity, the increased vascularity being impossible on account of the induration.

Chronic inflammation of the serous membranes is characterised by either mere opacity or by thickening with or without contraction, *i.e.* fibrous hyperplasia with or without induration.   There may also be distinct hyperplasia of the epithelium (or endothelium), which may even become converted into a kind of squamous epithelium.   Increased vascularity is often present, and with this hydrops is frequently associated, which followers of Heidenhain would be inclined to regard as due to an increased functional activity of the endothelium.   Here, then, all the four factors *may* be present, but the fibrous changes *always*.

When the lesions of chronic interstitial inflammation, *e.g.* interstitial nephritis, cirrhosis of the liver, interstitial myositis and myocarditis, are examined microscopically, the most striking feature is the marked fibrosis which has taken place—fibrous tissue, more or less well formed, and often of exceeding firmness, surrounds the active or organic structures, whether they be kidney tubules, liver cells, or muscle fibres; the framework or secondary elements may altogether outgrow the primary elements.   Increased vascularity is often present, but may be absent in advanced stages; a hyperplasia of the epithelial tissues cannot of course take place in myocarditis or myositis; but in the interstitial forms of chronic

inflammation it is generally absent, even in organs which are largely epithelial in structure, such as the kidney, liver, and pancreas. In an interstitial nephritis the renal epithelial substances become compressed and atrophied, the liver cells degenerate and disappear extensively in most forms of cirrhosis, and the pancreatic cells share the same fate.

As the acute inflammation, the result of bacterial irritation, passes off, if it has caused no serious lesion to the muscle fibres themselves, practically no permanent change may be left behind. If, however, the acute injury has caused serious lesion, breaking up some of the muscle fibres, or producing partial or total necrosis, then repair is accompanied by formation of fibrous tissue, and the foundation for a fibrous hyperplasia is laid. This newly formed fibrous tissue, endowed with the progressive stimulus characteristic of all infant growth, may extend beyond the original seat of lesion, between the sound muscle fibres, so that on transverse section at this stage small and compressed muscle areas, surrounded by rings of fibrous tissue, are seen, — "chronic interstitial myositis." The effect of this compressing fibrous tissue is to cause further degeneration of the muscle fibres, and, as these disappear, more fibrous tissue appears—the "vicious circle" is established. (2) Another cause of chronic interstitial changes in muscle is atrophy. When a muscle atrophies as the result of a central or peripheral nerve lesion, fibrous tissue may soon appear and take the place of the muscle fibres. "Tissue degeneration, if not repaired, leads to fibrosis"; degenerated muscle fibres are replaced by invading and proliferating connective tissue. Adami has spoken of this form of fibrosis as "a replacement fibrosis." It seems, therefore, that an important cause of progressive chronic interstitial myositis is the degeneration of the muscle fibres, which may be due (a) to an acute interstitial inflammation, or (b) to myotrophic or neurotrophic lesions, and which (c) may be kept up by, or progress with, the appearance of the fibrous tissue.

Similar conditions are met with in the so-called peripheral neuritis of diphtheria or lead poisoning. Sidney Martin and others have shown that the earliest stage in the process is a degeneration of the nerves; this is followed by a proliferation of the connective tissue, which may go on to fibrosis. In the spinal cord the degenerated tracts and areas are replaced by fibrous tissues. In these cases there is no sign of acute inflammation, no dilatation of the vessels, no appearance of new vessels, no leucocytic infiltration, but merely a degeneration which excites the connective tissue to proliferation, that it may replace the lost tissue. This is not inflammation, but a different process altogether.

In cirrhosis of the liver difficulties arise, since the intercellular, lobular, and biliary types differ so widely, and are so diverse in their etiology and histology; it seems impossible to explain them all in the same manner. When, however, any form of cirrhosis is so far advanced as to cause so marked a degeneration of the liver cells that recovery is impossible, then the degenerate cells may act as a further stimulus for progressive fibrosis. It appears that the primary cause of cirrhosis is *always* a degeneration of the hepatic cells caused by some toxine, such as owes its origin to alcoholic or syphilitic poisoning; and it appears that, when the process of cirrhosis has once begun, the degenerated cells are replaced by fibrous tissue, and that the degeneration is to some extent responsible for a continuity in the cirrhotic process. Obviously the connective tissue must be in a position to respond by proliferation before a fibrosis can result. If its activity be impaired, either because the whole individual is atrophying, or because it is itself hopelessly badly nourished, fibrosis cannot possibly take place.

Venous engorgement occasionally, though rarely, leads to induration; this induration is probably due to the engorgement, which causes degeneration of the organic cells; these cells are then replaced by proliferated connective tissue. Generally, however, the tissues are too badly nourished to respond by proliferation. Where general debility or impairment is absent, a fatty or waxy

metamorphosis of the liver may be accompanied by fibrosis, as in true fatty cirrhosis. Cirrhosis of the liver is always due to proliferative changes in the interstitial, portal, or lobular connective tissue, appearing to respond to cell degeneration, which promotes the progress of the fibrosis.

Ordinary interstitial nephritis (red atrophic kidney) may be produced by primary hyperplastic changes in the interstitial connective tissue; but it has yet to be proved that it is a primary hyperplasia, and not a hyperplasia called into existence by degenerative changes in the renal tissue. The chronic interstitial changes in a white kidney are certainly due to several factors—(a) the repeatedly recurring attacks of acute or subacute inflammation; (b) the organic destruction resulting therefrom, which awakens the connective tissue; and (c) the proliferative energy of the connective tissue.

The various forms of chronic inflammation may be reviewed shortly as follows : —(a) Processes which begin primarily in the connective tissue; fibrosis appears and progresses, the process being in part maintained by the destruction of the organic elements (*productive fibrosis* of Adami); (b) processes which begin with an atrophy of the organic elements, the latter being replaced by hyperplastic connective tissue (*replacement fibrosis*, Adami); (c) processes which, occurring on free surfaces, involve all structures concerned, but where again the most striking phenomenon is the fibrous hyperplasia, included under *productive fibrosis*, by Adami.

The important law is that "tissue degeneration, if not repaired, leads to fibrosis," provided of course that the connective tissue is capable of further growth—for if it be half dead itself, it cannot possibly assume fresh vigour—and provided also that the stimulus for proliferation is sufficient, or, adopting Grawitz's metaphor, that the connective tissue has been sufficiently roused and awakened.

"Is chronic inflammation an inflammation at all?" Inflammation is recognised by its appearances and phenomena, and *inflammation is not synonymous with repair.*

In microscopical specimens of tissues and organs undergoing so-called chronic inflammation, the appearances of inflammation are not found, but appearances characteristic rather of repair by fibrous tissue. True, at the outskirts of a chronically inflamed area, there may often be detected a few dilated vessels surrounded by clusters of round cells, but the bulk of the specimen shows nothing that could be called inflammation. Chronic inflammation, exhibiting all the changes of repair, cannot possibly be *inflammation, for inflammation ceases where repair begins,* and chronic inflammation is a term which has been given to conditions which already show *completed* repair, or which show *excessive* repair. This excessive repair—the hyperplasia and hyperplastic tendency of newly formed fibrous tissue—is an important element in some forms of "chronic inflammation."

An acute inflammation, in the language of the surgeon or physician, is frequently followed by a chronic inflammation. What does this signify? Merely this, that the effects of the acute process have been repaired by fibrous tissue, developed from the proliferating connective tissue; but the latter, once awakened to increased growth, in the full enjoyment of renewed vigour, continues to develop further and further on the slightest provocation. An acute inflammation is often the precursor of a fibrosis, but surely that is no justification for calling the resulting fibrosis a chronic inflammation.

An acute nephritis may at once pass into gradual and progressive induration (contracting white kidney) on account of such excessive repair. But in most cases where a fibrosis has followed upon an acute inflammation, there is an injured and dying tissue left behind, which acts as the proliferative stimulus upon a responsive and awakened connective tissue. And, what is still more important, in most cases the acute inflammation recurs from time to time, and rouses

the connective tissue to continued repair, when it is already in a condition of initial fibrosis, ready to proliferate, so that every fresh acute attack only makes matters worse. A fibrosis may therefore result from a single acute inflammation, or from repeated attacks of acute inflammation, but on this account it is not necessarily to be looked upon as an inflammation.

Instead of repeated attacks of inflammation, there may be repeated or continued irritation, which does not necessarily produce, or may stop short of producing, an inflammation. In most cases, no doubt, repeated irritation does lead to repeated attacks of inflammation, so localised and so slight that they are not recognised, subjectively or objectively, but are nevertheless sufficient to awaken the connective tissue to hyperplasia and fibrosis, and also to cause a hyperplasia of the epithelial elements, and an increased functional activity. But even then the inflammatory attacks themselves do not constitute the chronic inflammation; they simply incite to hyperplasia and hypertrophy.

In interstitial processes, especially cirrhosis of the liver and kidney, there is nothing suggestive of the presence of an inflammation; but there is fibrosis. It may be said, there is no evidence that this is the outcome of a previous inflammation, the processes appearing in the interstitial tissue, which has been awakened either by irritant substance, or by degenerating cells, or by a combination of the two stimuli. Possibly here and there an acute hepatitis or nephritis may have existed to begin with, but then it merely acted as the initial stimulus. The essence of the cirrhosis is the progressive fibrosis, which appeared either independently of an inflammation, or in the wake of an inflammation as excessive, or hyperplastic repair.

But it may again be objected that necrobiosis and necrosis in myositis produce inflammation, and that therefore tissue degeneration leads to inflammation, and that the term chronic inflammation is justified. That is only true to a certain limited extent, where large necrotic areas, infarcts, hæmorhages, and such like lesions are concerned, but is assuredly not true of progressive degeneration. Even infarcts and necrotic areas may disappear in a scar, without any actual or real inflammation ever having existed. The necrosed elements must first be removed. This may be done by a process of absorption or phagocytosis, with or without inflammation. The dead tissue having been removed, then the fibrous tissue fills up the gaps. If there is only one gap to fill up, a cicatrix is formed—repair—but that is not chronic inflammation; if, however, the necrosis or degeneration be both extensive and progressive, and is responded to by equally progressive reparative proliferation, then fibrosis ensues, or, in ordinary language, chronic inflammation.

Chronic inflammation, then, may be regarded as a hyperplastic change of the connective tissue, occasionally accompanied by hyperplasia and hypertrophy of the epithelial and glandular elements, produced either by repeated or continued irritation (extrinsic or intrinsic), or by a single and more often by repeated attacks of inflammation; it may be called into existence by progressive tissue degeneration, when the epithelial and glandular elements, of course, do not share in the hyperplastic process. An inflammation it is not, because, histologically, it is a process which is solely concerned with tissue elements which are considered characteristic of repair; inflammation is not even a constant precursor. It would therefore be well to abolish the term chronic inflammation from morbid anatomy and histology, if not from clinical medicine and surgery.

Chronic Inflammation (so called).

I. CHRONIC SUPPURATION (abscesses or ulcers).—Granulation tissue and continued irritation.

II. CHRONIC CATARRH.—Proliferation and increased functional activity.

III. INTERSTITIAL INDURATION $\left\{\begin{array}{l}\end{array}\right.$ Result of degeneration.
    (cirrhosis and sclerosis)   "   continued irritation.
                              "   cicatricial hyperplasia.

IV. SUPERFICIAL INDURATION $\left\{\begin{array}{l}\end{array}\right.$ Result of continued irritation.
    (mucous and serous   "   cicatricial hyperplasia.
    membranes)

REGENERATION AND REPAIR.

Tissues which are used up during ordinary normal wear and tear, or which have been destroyed by injury or other pathological processes, must be replaced or repaired if life is to continue, or if a cure is to be effected. Repair may be either direct and homologous (regeneration), or indirect and heterologous. Thus the cuticular cells, the epithelium of mucous surfaces, are constantly reproduced, new cells being developed to take the place of the old ones. This regeneration is purely physiological, and is a continuous process. Physiological repair is always homologous.

Under pathological conditions repair is more rarely homologous; as a matter of fact, it is more commonly indirect or heterologous. Still, it must be borne in mind that a tissue defect, whether due to injury, degeneration, or any other cause, may be made good by regeneration. Thus connective tissue, nerves, and vessels may be regenerated; but the power of regeneration varies considerably for the different tissues, and also for different animals. Thus, while certain low forms of animals are capable of reproducing whole complex organs, man and most warm-blooded mammalia are most restricted in their recuperative powers. Whole organs are never reconstructed in man, but only certain tissue elements. Epithelium and connective tissues, if the defect be limited, may be regenerated, the regenerative power being always most marked in the least specialised and differentiated cell elements. Thus ganglion cells are never reconstructed, and muscle fibres only rarely when there has been complete destruction; but when only a portion of a cell has been destroyed, the fragment may be restored, as *e.g.* the process of a ganglion cell. Again, tissues which have become mature and are permanent are less capable of regeneration than tissues which are more or less temporary and constructive. Thus the periosteum is more readily re-formed than cartilage. The regenerated tissue is always derived from homologous tissue, *i.e.* epithelium is derived from epithelium, connective tissue from connective tissue, muscle from muscle, etc.; connective tissue cannot produce epithelium. Regeneration obeys rigorously the law of specificity, *omnis cellula e cellulâ (epigenesis)*. Where homologous repair is absent, the defect is made good by the development of fibrous cr cicatricial tissue— the common form of repair. Injured or degenerated tissues, if not regenerated, are replaced by fibrous tissue, unless the organ is in such a condition that it is incapable of further proliferation. When an inflammation ends in resolution, there is direct repair or degeneration; when it ends in induration, indirect repair by fibrosis; when a degeneration such as is observed in peripheral neuritis passes off, and the affected portions recover themselves, true regeneration takes place; while, when the degenerated elements disappear, and their place is taken by fibrous tissue, there is an indirect repair, a patching up. It is erroneous to suppose that indirect repair is always accompanied or preceded by inflammation, or to define any attempt at repair, whether direct or indirect, as inflammation.

Since pathological repair implies increased proliferation, it will be readily understood why reparative tissue is so liable to hypertrophy; the proliferative stimulus may produce a more or less lasting effect or impression.

Repair.

I. Direct or Homologous—

(a) *Continuous* = physiological
{ Cuticle
Epithelial lining
Glands
Periosteum } Wear and tear.

(b) *Discontinuous* = pathological
{ Epithelium
Connective tissue
Periosteum
Nerves
Muscles } Injury or degeneration.

II. Indirect or Heterologous = pathological
{ Mature and permanent tissue, large areas of injured or degenerated tissues, highly specific tissues.

Repair must not be confounded with recovery. Homologous or *direct* repair is true recovery; there is a complete *restitutio ad integrum.* Indirect repair is something entirely different from recovery. First of all, it is not a *restitutio ad integrum;* secondly, it may not even be a cure. Often, no doubt, new-formed tissue acts as a barrier against the noxious agent, and encapsules the dead matter and entraps the *materies morbi* without doing harm to the organ and its function. Frequently, however, the elements of the organ suffer, its function becomes impaired, and the attempt at cure is as bad as the disease. Take, for instance, a fibroid heart, the fibrous tissue having resulted, let it be assumed, from a patching up of an interstitial myocarditis, still, the newly formed tissue weakens the heart, and serious symptoms, nay sudden death, may result. In physiological repair there is a limit beyond which matters do not progress in pathological repair, and especially when it is heterologous, the patching up may be carried to excess. (See " Chronic Inflammation," p. 35.)

METAPLASIA.

Metaplasia is a change of tissue type—a change limited and following certain laws; it is specific, but not generic, *i.e.* a connective tissue may change to another form of connective tissue, but never into epithelium, and an epithelium changes to another form of epithelium, but never to connective tissue. Metaplasia is naturally commonest in the pleomorphic tissues; therefore it is most frequently met with in the connective tissues. Physiological metaplasia may be seen in the development and growth of bone, in the formation of fat, and in the keratinisation of epidermal epithelium. In these instances the metaplasia is a continuous process; in some cases, however, it is discontinuous, called forth by certain stimuli. Thus, when the breasts become active, there is a metaplasia from cubical or short columnar epithelium to a secretory or glandular type.

Under pathological conditions the metaplasia of the connective tissue may be retrogressive or progressive. Cartilage may change into myxomatous tissue, and

fatty tissue into a fat-free œdematous or mucous tissue. These are instances of a retrogressive metamorphosis. On the other hand, cartilage may become bone, mucous tissue cartilage, or fibrous tissue bone; these are instances of a progressive metamorphosis. Tissue which has resulted from repair is extremely liable to metaplasia, and so is the tissue of certain new growths, namely, sarcomas. The delicate connective tissue which appears after pleurisy may change into dense and hard fibrous tissue, and the latter into bone or cartilaginous tissue.

As far as the metaplasia of the epithelium is concerned, under the influence of irritation, (a) columnar epithelium changes into squamous epithelium, and (b) squamous epithelium may become horny. But squamous epithelium never becomes columnar or ciliated. Examples of a metaplasia of columnar epithelium may be looked for in the larynx, nose, or uterus, where, as the result of so-called chronic catarrh, the columnar or ciliated cells change into the squamous type, and the latter may even become keratinous. This metaplasia of the epithelium is most important in connection with carcinoma. A cancer developing in transformed epithelium always adheres to the new type of epithelium, and does not revert to the original type.

Metaplasia.

I. PHYSIOLOGICAL—

    (a) *Continuous.*—Ossification, keratinisation, fibrosis.
    (b) *Discontinuous.* — Change in breast from resting to active state.

II. PATHOLOGICAL—

    (a) *Connective tissue.* — Retrogressive—cartilage to myxomatous tissue.
        Progressive — cartilage to bone.
    (b) *Epithelium.*—Columnar epithelium to squamous—squamous epithelium to horny epithelium.

HYPERTROPHY.

Tissues of organs and limbs may increase in size or enlarge under certain conditions, which may be either physiological or pathological. The increase in size, without structural changes, constitutes *hypertrophy*. Under physiological conditions, and with continued exercise, a muscle, or a group of muscles, may enlarge; the fibres increase both in number and in size. Similarly, the heart of an athlete may become slightly enlarged. It must be remembered that the body is so constructed that in health the organs are not worked to their utmost, and that they are capable, under exertion, of doing an increased or even an enormous amount of work; if these demands on the functional activity of the organs is kept up, they are capable of adapting themselves to the new requirements. Physiological hypertrophy is therefore a process of adaptation.

Under pathological conditions hypertrophy may show itself as the result of two altogether different processes—(a) it may be due to adaptation, *i.e.* compensatory hypertrophy; or (b) it may be due to an abnormal proliferative stimulus, the tissue or tissues growing and expanding without any extra demands being made upon them.

Compensatory hypertrophy is the more interesting and important form. On this power, which the body and portions of the body possess to adapt themselves to altered conditions, life, in health and disease, greatly depends, and when in disease the limit of compensation has once been reached, death soon supervenes. Compensation or adaptation may be so

complete that an individual seriously maimed may be able to live a long and useful life. Compensation is not exclusively hypertrophic. It may be merely functional or vicarious, one organ supplementing another. Compensatory hypertrophy may be—(1) Supplementary, upon an increased demand for work; (2) vicarious, affecting a whole organ after loss of one of a pair of organs, or a portion of an organ after a partial loss of substance; (3) systemic, where a lesion is counteracted by a complete readjustment of several or even numerous organs or tissues. Thus, if there is obstruction to the outflow of urine, the bladder wall may become considerably thickened, this being due to an increase of its muscular substance; or, again, if there is an obstruction of the aortic valve, the left ventricle becomes thickened, more force being required to propel the blood through the narrowed opening. So long as the hypertrophy is adequate, matters may progress so well that all symptoms of disease are practically absent. A good example of vicarious hypertrophy is the enlargement of one kidney after removal or total obstruction of the other, or enlargement of a part of a kidney after atrophy of the remainder. The best example of systemic hypertrophy is also found in renal diseases, as with granular kidney when the left ventricle of the heart hypertrophies and the tunica media of the arterioles increases in thickness.

The increase in size is due chiefly to proliferation of the tissue constituents, without change of structure, but they may also become enlarged. It is customary in theory to distinguish between hypertrophy and hyperplasia. In either case the type and structure of the tissue remain unaltered; in hyperplasia there is a numerical increase of the tissue elements, in hypertrophy an increase in volume. Since, however, hypertrophy is always accompanied by hyperplasia, it is best to call any increase in size without histological change hypertrophy, even though this may not be quite accurate, for it is impossible to draw a hard and fast line between the two processes.

Hypertrophy or overgrowth may be either primary or secondary. *Primary overgrowth* may be due to irritation, or possibly to long-continued hyperæmia and certain nervous changes (pseudo-hypertrophic paralysis), but its cause may be altogether obscure; again, it may involve a whole organ, *i.e.* all its components, or only some of them. A whole extremity or a finger or toe may overgrow, and then all the components are hypertrophied; on the other hand, as in elephantiasis, the skin and subcutaneous tissue only may increase. Again, a breast may hypertrophy generally, or only its fat or glandular substance may develop abnormally. When the cause of the overgrowth is obscure, there may have been (1) congenital influences (moles, nævi, ichthyosis); (2) disease (nails and teeth); or (3) arrested involution (uterus and breast), but often even then no explanation can be found (lymphadenoma and goitres).

In secondary overgrowth a new tissue is first produced, either as the result of irritation, inflammation, or atrophy, metaplasia or heteroplasia, and this new tissue then overgrows. As examples, the formation of keloids and exostoses, developing in common with muscular and tendinous insertions, may be mentioned; again, fibrous tissue may appear as the result of atrophy (cirrhosis of the liver, senile changes in the breast), and this tissue may undergo considerable proliferation, a so-called hypertrophic condition being produced.

PATHOLOGY OF BACTERIAL INFECTION.

In the causation of diseases and morbid lesions, minute vegetable organisms play an important part.

CHARACTERS OF BACTERIA.

Classification.—The pathologist, awaiting the final classification of the botanist, temporarily arranges the vegetable bacterial organisms in morphological groups, and he uses terms which, from a botanical point of view, may be objected to, but which have become customary, and will probably be adhered to until the botanists have settled their disputes. Vegetable micro-organisms are roughly divided into (1) fission fungi, or bacteria, (2) sprouting or budding fungi, and (3) mycelial fungi, of which the bacteria are the lowest and simplest forms, and the mycelial fungi the highest and best developed. Most disease-producing organisms belong to the first group, a few only to the third. The budding fungi include the yeasts which are responsible for certain processes of fermentation, and are also said to cause tissue irritation.

The fission fungi, according to their shapes, are again divided into three main groups :—

1. **Cocci.**—Globular, subglobular, oval, ovoid, or reniform.

    (1) *In chains*—
        (a) Streptococci . . . $\left\{ \begin{array}{l} Pyogenes \text{ and } erysipelatis. \\ Pneumoniæ. \end{array} \right.$

    (2) *In pairs*—
        (b) Diplococci . . . $\left\{ \begin{array}{l} Pneumoniæ \text{ (meningococcus)}. \\ Gonorrhœæ. \end{array} \right.$

    (3) *In tetrads*—
        (c) Tetracocci . . . . *Micrococcus tetragenus.*

    (4) *In three dimensions*—
        (d) Sarcinæ . . . . $\left\{ \begin{array}{l} Pulmonalis. \\ Ventriculi. \end{array} \right.$

    (5) *In irregular clusters*—
        (e) Staphylococci . . . $\left\{ \begin{array}{l} Pyogenes \text{ } aureus. \\ albus. \\ citreus. \end{array} \right.$

The streptococci are arranged in chains, varying considerably in length, the diplococci in pairs, the tetracocci in fours, the sarcinæ in groups of fours, and the staphylococci in irregular masses. This classification, based on the method of division, though useful, is extremely imperfect, because it is not exclusive. Thus the diplococcus is at the same time the simplest form of streptococcus or of staphylococcus. The pneumococcus, which in pneumonic sputum generally occurs in encapsuled pairs, in artificial media grows as a streptococcus; the *Micrococcus tetragenus*, which in phthisical cavities is found in fours, surrounded by a capsule, in artificial media becomes a staphylococcus; so also do most sarcinæ.

2. **Bacilli** include all rod-shaped organisms. They are generally long or short straight cylindrical cells with rounded, pointed, or straight ends, but some of them are clubbed and evince a tendency towards branching. The latter, strictly speaking, should be taken out of the group of bacilli, and placed amongst the mycelial fungi in a class by themselves; they are, however, as a rule kept in this group. The following bacilli are found in association with disease in man:—

(1) *The straight bacilli—*

Bacillus of anthrax.
"   " glanders.
"   " typhoid fever (motile).
"   *coli communis* (motile).
"   of   malignant   œdema (motile).
"   " blue pus (motile).
"   " tetanus (motile).
"   " influenza.
"   " plague (motile).
"   " Friedländer (motile).

(2) *The clubbed or branched bacilli—*

Bacillus of tuberculosis.
"   " leprosy.
"   " tetanus (motile).
"   " diphtheria.
"   " xerosis.

Bacilli may be motile or non-motile. When motile they possess flagella, which may be distributed all round the organisms, as is the case with the typhoid and tetanus bacilli; or they may be fixed at one or both poles, *e.g.*, bacillus of blue pus. There is no correlation between the rapidity of movement and the number of flagella, but it is generally held by botanists, who divide the bacilli according to their flagellation into *Monotricha* (a single termal in flagellum), *Amphitricha* (a single flagellum at each pole), *Lophotricha* (a bundle of flagella at one pole), and *Peritricha* (surrounded by flagella), that the arrangement of the flagella is a specific character.

Bacilli always divide by transverse fission into (*a*) paired bacilli, and (*b*) filamentous forms, of which the anthrax bacillus is a good example. Many bacilli are capable, before they die, of producing endogenous spores, which are highly refractive bodies, spherical or ellipsoid, developing in the interior of the cell substances. These spores are highly resistant to the action of physical and chemical agents, and may be (1) central (anthrax bacillus), or terminal (tetanus bacillus), or indefinite. The spore placed in favourable conditions again grows into a bacillus. The following pathogenetic bacilli are sporogenous:—(1) Anthrax (central sporulation). (2) Tetanus bacilli (terminal sporulation). (3) Malignant œdema. None of the pathogenetic cocci or spirilla which occur in man, sporulate.

3. **Spirilla.**—The third morphological group consists of the vibrios— short, small, comma-shaped organisms, and the spirilla of longer, tortuous, or screw-like threads. The vibrios may be linked in such a way as to produce a jointed spirillum or an S-shaped curve, or they may grow into true spirilla. They are mostly motile and flagellated. The most important vibrio or spirillum, from the pathogenetic point of view, is that of Asiatic cholera; spirilla and vibrios, however, occur commonly enough in the intestinal contents, the mouth, tonsils, and nose, and are often found in diarrhœic stools.

Involution, Pleomorphism, and Variability.—Bacilli, cocci, and spirilla, when kept in or on artificial media, or even while growing in the animal organism, frequently show changes in their morphological appearances. In young cultures of an organism the different individuals resemble each other very closely, but as the culture becomes older, irregular and typical forms appear; this is degeneration or *involution.* Such degenerate forms, transplanted on good and fresh soil, will again resemble the true or original type. Vibrios when grown on agar-agar or in other media frequently become coccoid; other organisms swell up with age or become segmented. In other cases, *e.g.* diphtheria and tubercle bacilli, there may sometimes be noticed in young and perfectly fresh cultures

curious clubbed or branched forms. These organisms are therefore supposed to be closely related to the streptothrix forms, the appearance of branched forms affording an example of a progressive metamorphosis. *Pleomorphic* organisms even in young cultures show variety of shape, the pleomorphism being a distinctive character of the species.

Pleomorphism and involution must not be confounded with variability. On changing the external conditions and soil an organism will vary somewhat, not only in its morphological, but also in its biological characters; a short bacillus may become long, and a pigment-producing organism may lose its chromogenetic power. Variability is possible only within very narrow limits. Morphologically an organism may vary in shape, but the limit of its variability is fixed by its genus; thus cocci remain cocci, bacilli remain bacilli, and spirilla remain spirilla. Pleomorphic organisms retrogress or progress to a higher or lower class, *i.e.* an irregularly-shaped bacillus may become clubbed or branched. We still speak of diphtheria, leprosy, or tubercle bacilli, but it is questionable whether these are bacilli at all, and do not rather belong to a special genus. Singling out the established genera amongst the vegetable organism, the constancy of form upheld by Cohn and Koch must be accepted; cocci, bacilli, and spirilla do not change one into the other, and even amongst the cocci such main divisions as streptococci and staphylococci are not interchangeable.

Variation can be achieved by artificial cultivation, and the result may be (1) a temporary, (2) a more or less permanent, and (3) an absolutely permanent variety. If a variety is temporary, on restoring the old condition, reversion to type quickly follows, while, as the endurance of the variety increases, the liability to reversion diminishes. Variation is generally due either to degeneration or to adaptation to a richer or better soil: in the former case variation is an easy matter, but in the latter variation is much slower and can often be produced only by a process of selection, that is, by constantly selecting colonies presenting the features which it is wished to emphasise. Variability shows itself generally in the following directions:—(a) *Mode of growth*, namely, changes in rapidity of development, in the amount of liquefaction, in the size of the colonies, and in the amount of mucilaginous material; (b) *temperature*—organisms may become accustomed to a higher or lower temperature than that at which they grow best; (c) *oxygen requirement*—aërobic organisms may be trained to grow under anaerobic conditions, and conversely anaerobic organisms may be accustomed to aërobiosis; (d) *resistance to antiseptics;* (e) *bio-chemistry*—an enzyme may be lost or acquired by change of medium, a pigment lost or acquired, and a toxine increased, diminished, or lost altogether; (f) *sporulation*—an organism may be so modified that it loses its power of forming spores. It is important to note that, in the instances given, variability mostly implies loss of something, rarely the acquisition of a higher function. Again, variability is far oftener physiological and biochemical than morphological. It is quite easy to alter the shape of a bacillus or spirillum and the grouping of bacteria by a change of medium, but then this change is almost always temporary, and it affects only a larger or smaller proportion of the organisms growing on or in the medium. Taking it altogether, there is as yet no reason to give up the belief in the constancy of form. Physiological and biochemical properties do vary considerably, not only under artificial conditions, but most probably also in nature, and it is more than possible that an organism may for some reason or another suddenly acquire pathogenetic properties.

REQUIREMENTS OF BACTERIAL LIFE.

Bacteria require oxygen, nitrogen, carbon, hydrogen, oxygen phosphorus, and salts, which may be supplied in various ways. Nitrogen may be supplied in the form of diffusible albumins and peptones, or in the form of non-albuminous substances containing an NH_2 or NH group

(leucin, asparagin, etc.), or even in the form of nitrates. It is important to remember that pathogenetic germs may be cultivated in non-albuminous solutions, because this proves that organisms work up their poisons in their own substance, and not by splitting up the solution in which they grow. Carbon may be supplied either with the diffusible albumins and peptones, or in the form of sugar or other carbohydrates, glycerin or fat; it is obtained from the above substances. Phosphorus may be given as phosphates, but is generally present in the ordinary albuminous substances used.

The oxygen requirement.—The pathogenetic organisms may be divided into three groups, according to their behaviour towards oxygen. Some organisms, *e.g.* bacillus of tetanus or bacillus of malignant œdema, grow in an atmosphere devoid of oxygen, and, so far as the best evidence goes, cannot grow in the presence of *free* oxygen, they are therefore *obligatory anærobes*. Others require the presence of free oxygen, and are *obligatory aërobes;* but the majority of bacteria are facultative anærobes, *i.e.* they are capable of growing in an atmosphere devoid of oxygen, and also in the presence of free oxygen, some growing better without—others better with it. Most pathogenetic organisms which in the laboratory grow as aërobes, in the body produce their lesions and diseases as anærobes, for in the tissues there is no free oxygen. Pasteur thought that bacteria and yeasts developed their fermentative and chemical activity best in the absence of oxygen. This does not appear to be an absolute law, although it cannot be denied that the absence of oxygen often provokes a more intense fermentation. Further, many of the organisms which in the tissues are anærobic can, outside the body, be grown without oxygen only with difficulty or not at all. This shows how imperfectly the test tube supplies the conditions existing in the living body. (2) The range of temperature at which bacterial life is possible varies considerably. There are organisms which grow at a low temperature, under 15° C., others which can only grow at a temperature of the human body and up to 40–42°·5 C., and others again which grow at any temperature between 10° C. and 42°·5 C. The most extraordinary are the thermophilic organisms, found in fæces, which only develop at temperatures above 45° and up to 60° C.; they appear, however, to be of no pathological importance. All pathogenetic organisms are capable of growth at blood temperature; some readily perish if kept below this temperature; others, however, persist either in a vegetative form, or as spores, or in a dormant and latent condition, often retaining their full virulence. Thus the staphylococci of suppuration thrive well at low temperatures, as does the typhoid bacillus; the bacilli of anthrax and tetanus form spores; while the tubercle bacillus and streptococci retain their vitality, the latter even when kept in an ice chest. Again, higher temperatures may be borne by many organisms, either by virtue of their own natural resistance or by their power of sporulation. Many pathogenetic organisms, then, possess a strong vitality, the far-reaching importance of which fact will be evident. (3) Light, generally speaking, is harmful to most pathogenetic organisms, either destroying them outright, or at least attenuating them, or modifying them. Direct sunlight is infinitely more potent than diffuse light, and the actinic more powerful that the heat rays. Apparently contact with free air is necessary for the perfecting of this action, and it is believed that the sunlight in the presence of free air produces either ozone or H_2O_2, and that the bacteria are destroyed by these substances.

(4) High altitudes and great atmospheric pressure are inimical to the development of pathogenetic germs.

It is important in all cases to study the effect of surroundings and physical conditions on disease-producing organisms, because it is evident that a resistant germ is a much more difficult foe to grapple with than one which is very sensitive.

Vital Manifestations of Bacteria.

It is evident that chemical changes take place during bacterial growths, for nutrition depends on them; energy is developed as a result of such growth. Nutrition has two objects to fulfil—(a) to supply the bacteria with food material for their own development and proliferation; (b) to supply the substances required for the development of energy. For mere vegetation plastic nutriment alone is necessary, *i.e.* simple substances; but for the display of energy, additional food material, and additional chemical substances are required.

A change of medium or surroundings may alter the activity of an organism; virulent bacteria after their removal from the body may become attenuated, and organisms which generally merely vegetate on the mucous or other surface of the body may under certain conditions acquire marked virulence. A virulent streptococcus can be kept for a long time in vegetative form on gelatin in a refrigerator, so that when again injected into the animal body it once more gives unequivocal evidence of its virulence. The pneumococcus on a mucous membrane, so long as it is merely supplied with plastic food material, simply vegetates in a harmless way, but a change of conditions which implies a change of medium will cause it to display an unexpectedly virulent activity. Nutrition, whether for the purpose of vegetative growth or for the purpose of developing energy, is a process of assimilation, *i.e.* of synthesis, but this must always be accompanied by an output of certain substances. The latter includes (a) waste products, and (b) the products of intracellular chemical activity, *i.e.* secretions, which are often capable of calling forth fresh chemical processes.

Bacterial products.—By these are understood, generally, the sum total of substances which are found in a medium in which the bacteria have grown for some time. Hence they evidently include both the excreta and the secretions of these organisms. The medium may be altered in many ways—(1) organisms, growing in broth, use up certain substances, and hence alter the chemical nature of the broth, by removing them; (2) they may destroy others by splitting them up; (3) the excreta may form new compounds with substances found in the broth; (4) the secretions, especially if of the nature of enzymes, may by their action lead to the formation of a new series of molecular changes, which will greatly alter the medium; and (5) the organisms may act as ferments, and still further alter the medium. Hence the chemical activity of an organism is extremely diverse, and depends on a number of often highly complex processes, our knowledge of which must necessarily be at present both limited and crude.

Amongst the numerous so-called bacterial products may be found the following substances:—(1) Gases, (2) water, (3) nitrates and nitrites, (4) sulphur, (5) volatile bodies, (6) oxy-acids, (7) sulpho-acids, (8) amido-compounds, (9) aromatic bodies, (10) indol, (11) pigments, (12) carbohydrates, (13) peptones and albumoses, (14) ptomaines and so-called alkaloidal substances, (15) toxines and toxalbumins, (16) enzymes, (17) the extracts of the dead bodies of the bacteria, and (18) other

products of fermentation. All these substances are not found at once in the chemical products of one and the same organism, but this extraordinary multitude and diversity of the bacterial products must be borne in mind, because they show what the organisms may do, and how diverse, in disease, the phenomena due to bacterial intoxication may be. A few chemical processes, which have some bearing on health and disease, may be instanced:—(a) Organisms may be strong reducing agents, and may thus assist complex physiological processes. Thus putrefaction is essentially a reducing process, and whether it is absolutely necessary or not, putrefaction certainly assists digestion and absorption, and prevents intoxication from the intestinal tract. (b) Nitrates are reduced to nitrites, an indispensable preliminary process in nitrification, which, if not absolutely necessary for some forms and phases of vegetable life, yet is of great use to them. By nitrification ammonia is changed into nitrates; this process is a double one—(a) one group of organisms changes ammonia to nitrites, and (b) a second group changes the nitrites into nitrates. The nitrifying organisms are frequently associated with the leguminous plants, which use them for their own development. They can, however, do without them when ammonia or nitrates are present in sufficient quantity. This shows that, although not essential to life, these organisms, under ordinary conditions, are of the greatest use. It may be that bacteria are not essential for subsistence and growth, but by a process of adaptation the animal organism may, for the purpose of nutrition, have learnt to avail itself of the assistance of bacteria. Putrefaction, which normally takes place in the intestinal tract, and may reasonably be regarded if not as an essential as a useful process, as aiding in the splitting up of complex bodies, and in the destruction of poisonous bodies, is of course due to bacterial action, and is a complex chemical process resulting from bacterial fermentation, *i.e.* not a simple fermentation, but a compound fermentation. The following steps may be distinguished:—(a) The albuminous substances are changed by some bacteria into peptones and albumoses, by what appears to be a process of hydrolysis; (b) these peptones and albumoses are then split and changed into amido-acids and amides, nitrogenous aromatic bodies and sulpho-acids (such as taurin) also making their appearance; (c) the amido compounds are then decomposed into ammonia and fatty acids; (d) the ammonia is then altered by bacteria, as described under nitrification, and the fatty acids are split into CO_2, H_2, and CH_4. The products of putrefaction vary with the bacterial flora, and also with the presence or absence of oxygen. If oxygen is absent, true putrefaction takes place; if it is present, decomposition characterised by an absence of the bad and offensive odour, and frequently accompanied by reduction of the nitrates (dentrification), by which N_2 may be split off.

Fermentation may be brought about by (a) non-organised substances, the products of secreta (excreta) of bacteria, the enzymes, or (b) by the living bacteria themselves, which then act as true ferments. The enzymes may be isolated from the living bacteria, of which they are the products, and are characterised by the following points:—(a) They are capable of splitting up H_2O_2; (b) they are extremely sensitive to external influences—in the moist condition they are readily destroyed by heat, in the dry state they resist 100°–160° C.; (c) certain salts, such as aluminates and phosphates, and nitrogenous substances—asparagin—assist the enzymes in carrying on their fermentative activity; (d) they are more resistant to external influences while active, especially in the presence of neutral salts (sulphates); (e) they set up hydrolytic action, during which one or more molecules of H_2O are taken up, and a molecule of the fermenting substance is split into two or more molecules of a simpler substance; (f) they act on certain special substances only, and show a selective power as striking as that shown by the living micro-organisms; (g) their quantitative action is considerable, but by no means unlimited, the enzyme apparently forming

an unstable compound with the products of decomposition, which is easily split up, and the enzyme again set free on the addition of fresh material. The enzymes are closely allied to the toxines of disease-producing organisms, and for that reason they deserve special consideration. The following enzymes have been isolated from living bacteria :—

Amylase, which converts starch into sugar (diastase), found in anthrax bacilli, and the vibrios of cholera and of Finkler-Prior.

Invertase, which converts cane sugar into dextrose (found especially in yeast cells).

Glucoside enzymes, splitting glucosides into dextrose, and a body of entirely different composition.

Cellulose enzymes, capable of dissolving cellulose.

Peptonising enzymes, converting albuminous substances into peptones and albumoses (found in all organisms which liquefy gelatin).

Milk curdling enzymes, found notably in the *Bacterium coli.*

Urea enzyme, found in the *Micrococcus ureæ,* which converts urea into ammonium carbonate, hippuric acid into glycocol and benzoic acid.

Fat-splitting enzymes, splitting neutral fats into glycerine and fatty acids.

All these enzymes may be obtained from the bodies of micro-organisms. Thus, on destroying yeast-cells in a watery suspension by shaking them up with chloroform, invertase remains in suspension. The enzymes may display their activity either outside the cell (extracellular), or in the cell (intracellular) enzymes. An extracellular enzyme is secreted or excreted by the cell, and then works upon the material in which the cell is suspended, while an intracellular enzyme acts upon the material taken into the cell substance, splitting it up by a process of hydrolysis. The opinion is gaining ground that under normal conditions the enzyme action takes place in the interior of the living cell. Thus living and normal yeast cells do not give off invertase, but the inversion takes place in the cell body; only when the cell dies is the inversion given off, just as in fermentation, where the process is assumed to be a vital one, *i.e.* an intracellular one, although in other respects it closely resembles zymotic action. Thus a few organisms will produce an effect out of all proportion to the number of living organisms used; in both cases a definite medium of a certain chemical composition is required. Ferment action and enzyme action are so closely allied that it may be doubted whether they are really two distinct processes. Hitherto, for instance, it has been believed that the yeast cell, by some vital process, changes glucose into alcohol. Recently, however, an extract has been prepared of yeast cells, which, in the absence of all living cells, is capable of fermenting sugar solution. The great difficulty has been to separate this substance from the cell. We must therefore believe that the yeast cell takes up sugar, and, by means of an enzyme-like body in its substance, splits it up into alcohol and other substances, just as invertase in the cell substance inverts cane sugar. The yeast cells therefore build up two enzymes—(*a*) invertase, and (*b*) alcoholic enzymes, of which the former is easily given off, while the latter is obtained with much greater difficulty. Sugars are taken up by the living cells, and cane sugar inverted by the appropriate enzyme in the substance of the living cell, and either given off again as glucose or at once changed into alcohol by the other intracellular enzyme. It is legitimate, in the present state of our knowledge, to assume that the processes which are brought about by pathogenetic bacteria are comparable to those of the yeast cell.

The yeast cell (*a*) will only develop its fermentative power on suitable media : on others it will merely vegetate without giving evidence of its energy. (*b*) In a suitable medium its energy depends upon and varies with such conditions as absence of oxygen, concentration, accumulation of the products of fermentation and of waste. (*c*) Although fermentation varies with the rapidity of proliferation on the part of the yeast cell, alcoholic fermentation will still take place, when the cells have ceased to multiply; it appears that first the cell reaches its maximal vegetative energy, and then unfolds its maximal fermentative energy. (*d*) The yeast possesses two fermenting substances, of which one is of nutritive or plastic importance, namely, the invertase, which the cell will only use when it is placed in an unsuitable sugar solution; whilst the other is of specific importance, is firmly fixed in the cell substance, and is only separated with difficulty. This latter substance acts on certain chemical bodies absorbed into the cell, and then the latter give off an elaborated product, which may be regarded as the specific toxine of the yeast cell, namely, the alcohol. By way of an example, take the diphtheria bacillus. The latter may vegetate on the tonsil as a saprophyte, without producing any lesions; under certain conditions it becomes virulent, multiplies rapidly, and then displays its energy. It forms, if necessary, albumoses by an enzyme, and at the same time takes up substances from the nutrient material, and elaborates these into the diphtheria toxine, which is the specific product; the albumoses are of secondary importance, and will not appear, for instance, when the bacillus is grown in a solution of asparagin. Disease-producing organisms elaborate poisonous substances, which call forth certain symptoms, of which some are specific, and belong exclusively to a particular species, while others are general and shared by many organisms. The poisonous substance obtained from a tetanus culture, for instance, which, when injected into an animal, produces tetanus, is the specific poison; other poisonous substances, which merely produce fever and other general symptoms, are not specific, and may be found in many other organisms. It is a matter of the greatest importance to keep in mind this twofold nature of the poisonous substance of disease-producing organisms.

Ptomaines.—The ptomaines are nitrogenous bases, which bear some resemblance to the vegetable alkaloids; they are frequently described as cadaveric or animal alkaloids. Brieger divided them into two groups— the toxic and the atoxic ptomaines. He succeeded in obtaining from putre- fying material and from pure cultures of bacteria on meat, both forms of ptomaines. Most of the atoxic ptomaines are amines—cholin, neuridin (putrefying meat), gadinin (putrefying fish), putrescin, and cadaverin, but the toxic ptomaines are also closely allied to the amines; the best known of these are neurin, muscarin, mytilotoxin, and tyrotoxicon. Brieger obtained poisonous ptomaines from cultures of the *B. typhosus*, the cholera vibrio, and the bacillus of tetanus, and at one time believed that the specific toxines were ptomaines; but ptomaines have not been found in all patho- genetic cultures, whilst quantitatively they are present in such a small amount in others, that it is impossible to regard them as being the specific toxines. During putrefaction ptomaines appear, and since this takes place both outside and inside the alimentary tract, poisoning may be produced either through ptomaines ingested with food, or through ptomaines developed in the alimentary tract after the ingestion of food. The term "ptomaine poisoning" is often employed without there being sufficient evidence to justify its use, and it must also be remembered that the process

of analysis offers numerous sources of error arising from the extremely complicated nature of the chemical manipulation.

When Hankin and Sidney Martin discovered *toxic albumoses* in anthrax cultures, the specific poisons were thought to be albuminous substances which were called *toxalbumins*. In diphtheria cultures a poisonous body resembling serum albumin was found, and separated by Brieger and Fränkel; in other cultures, globulin-like substances; in others, again, toxic peptones, so that distinctions were made between toxalbumoses, toxoglobulin, and toxopeptones. All these substances were included in the term "toxalbumins." The latter undoubtedly contain *specific toxines*, since, on injection, they reproduce the specific lesions or symptoms of the infection; but the question which was soon raised was, whether these toxalbumins were pure substances or a mixture of albuminous bodies with the toxine. Thus Roux and Yersin separated from diphtheria cultures a specific toxine which appeared to be an *enzyme*. Previously chemists had pointed out that it was necessary to work with culture fluids containing known substances, and to free the bacterial products as thoroughly as possible from albuminous substances. Recent work has shown that when an attempt is made to precipitate the toxines from albuminous solutions, the toxines are carried down mechanically with the globulins, albuminoses, or peptones; and therefore, according to the constitution of the culture medium, the same bacterial toxine at one time may appear to be a globulin, at another time an albumose, and that, as a matter of fact, the worker has usually, if not always, to deal with mixtures of toxine and albumose or toxine and globulin. When diphtheria bacilli are grown in an albuminous solution, there appears, as shown by Sidney Martin, a mixture of albumoses, but, as shown by Uschinsky, in a medium free from albumin, a toxine free from albuminous matter is obtained, whilst Brieger and Cohn have succeeded in purifying the toxines of tetanus and diphtheria from all albuminous admixture, and Dr. Martin has extracted from the tissues of animals dead of tetanus, a toxine which is certainly not an albuminous substance.

These purified toxines undoubtedly resemble the enzymes in some respects, but they cannot be grouped with the enzymes, because their activity is essentially diffused and their action narrowly limited by the dose employed, while zymotic action is out of all proportion to the dose of enzyme used. It may be assumed, however, that the specific toxines are products of the bacterial cells, which take up certain substances, work them up into toxines, which are then excreted or secreted, and that the albumoses, globulins, etc., are merely secondary products due to the action of accessory enzymes.

Amongst the non-specific bacterial products the most important are the proteins of Büchner, apparently identical with Klein's *intracellular poison*, while the latter's *extracellular poison* is practically the same as the specific toxine. The proteins are the protoplasmic substances of the bacterial cells, and may be obtained by taking masses of bacterial cultures grown preferably on solid media, such as potatoes, agar-agar, and gelatin, destroying them by heat, and extracting them by alkalies or other chemicals. The nature of these proteins is not as yet clearly understood; some observers believe that the proteins of the different bacteria are identical in nature. This, however, is certainly erroneous, because the immunity produced by injection of the so-called proteins is strikingly specific, and it is probable that what are usually called proteins are mixtures of different bodies, amongst which even the specific toxines in small quantities may occur. It seems, however, that there are also other substances, found in many bacteria, which are non-specific in their action, and are capable of producing febrile symptoms, leucocytosis, inflammation, and other general changes. It must be clearly borne in mind that the pathogenetic bacteria, besides secreting toxines, are themselves poisonous, and that this coexistence of specific and non-specific poisons explains the difference and diversity of symptoms in infective lesions, of which some are

specific and others general and non-specific. The chemical changes that go on in a test tube are extremely complex, and those in the body must be equally, if not more so.

INFECTION.

There are a number of infectious diseases or lesions which never occur without the presence of micro-organisms in the tissues or in the body cavities. An infection must be defined as a morbid change produced in the body by bacteria, and a disease or a lesion is infective or infectious if it be thus produced. An organism capable of manifesting its presence by infection is a pathogenetic organism. Bacteria may be roughly, but not absolutely, divided into pathogenetic and non-pathogenetic. Every organism, even the most harmless, when injected subcutaneously in sufficiently large doses, will produce an inflammatory lesion. Again, an organism may be harmless to one species of animal and virulent to another; harmless to one individual and virulent to another; or in the same individual harmless under certain conditions, virulent under others. There are organisms which, when injected into an animal, in reasonable quantities, make no attempt at proliferation, but from the moment of inoculation steadily decrease in number without producing any symptoms of intoxication. Such organisms are non-pathogenetic.

Nature of infection.—The following are the known and recognised pathogenetic organisms capable of infecting man:—Bacilli of anthrax, diphtheria, glanders, tubercle, leprosy, typhoid fever, tetanus, malignant œdema ; and of Baltic fever—the pyogenetic cocci, including the pneumococcus and gonococcus, the vibrio of cholera, besides others whose exact position is as yet more or less ill defined. For a number of diseases which are probably infective, the bacteria have not as yet been discovered, *e.g.* syphilis, measles, scarlatina, variola, and certain other exanthemata.

Organisms in general, and especially the pathogenetic species, may be divided into *parasitic* and *saprophytic* organisms. The former are such as are capable of growing in living tissues; the latter thrive in or on dead or devitalised matter. Amongst the parasites, some, under certain conditions, may do well in or on dead matter, and conversely amongst the saprophytes there are some which, under certain conditions, are capable of growth and proliferation in living tissues; these organisms are the facultative saprophytes and facultative parasites respectively. Since most pathogenetic organisms grow in ordinary laboratory media, it is evident that they are mostly facultative saprophytes; but there is great diversity of opinion regarding their ability to thrive on such soils. An organism which cannot grow on dead matter is an obligatory parasite, and one which cannot grow on living tissues an obligatory saprophyte. There are but few obligatory parasites. However relative the terms saprophytic and parasitic necessarily must be, it is of importance to adhere to them. Many organisms may grow on the different mucous membranes, or on the skin as saprophytes, *i.e.* they there vegetate on the secretions or dead cells, but do not penetrate into the living tissues, and for the time being are not parasitic. Thus the pneumococcus is frequently found on the buccal or tracheal mucous membrane, where it grows as a saprophyte in the saliva or mucus without producing its active toxine, or evincing any tendency to infiltrate the underlying tissues. Similarly the *Streptococcus pyogenes* is found on the tonsils and elsewhere as a harmless inhabitant, *Staphylococci albi* and *aurei* vegetate on the skin, and in the

sebaceous follicles; and all sorts and conditions of micro-organisms lead a saprophytic and atoxic existence in the cavity of the alimentary canal. Some change occurs, either in the micro-organism itself or in its surroundings, which causes it to manufacture its toxine, and possibly at the same time to invade the underlying tissues. This change may be an alteration of the medium in which the organisms grow, for we know that the yeast cell, for example, can grow on gelatin without manifesting its fermentative activity; it merely vegetates; but on transferring it to a glucose solution, it at once begins to form alcohol. Again, organisms capable of secreting diastatic enzymes will often refuse to do so if albumin be present in the medium in which they grow; they require for their diastatic activity free oxygen and carbon in the form of carbohydrates.

An organism may therefore for a long time simply vegetate harmlessly, and then suddenly, by a process which may be compared to fermentation, it may produce toxine; and the latter, on being absorbed into the lymphatic and hæmic circulation, will produce symptoms of disease, *i.e.* the organism becomes pathogenetic. The organism in its new character may invade the tissues and become parasitic, or it may remain saprophytic, and grow on the surface of the skin or mucous membranes. Saprophytic organisms may therefore be exquisitely pathogenetic if they multiply rapidly enough and manufacture toxines in sufficient quantity to produce either local changes or general intoxication. Thus it may be granted that the *Bacillus coli communis* and anærobic organisms of certain kinds are normally present in the intestinal tract in limited numbers; these may for some reason or another increase enormously in number, and while still remaining in the lumen of the intestine elaborate a large amount of toxine, this leading to grave symptoms of collapse and prostration, and to diarrhœa and enteritis. On the other hand, organisms may find their way into the intestines from without, as for instance the cholera vibrio, which may grow and multiply on the mucosa without invading it, and as a saprophyte produce a copious amount of poison, which, on being absorbed, leads to the most serious symptoms.

Streptococci which vegetate on the tonsils in a harmless form, or as atoxic saprophytes, may become exquisitely parasitic, and invade the tissues of the tonsil; their toxines may be absorbed, and fever with other grave symptoms result; nay, they may find their way into the lymphatics and the general circulation, and produce a general septicæmia. Pneumococci, through the changes produced by cold and exposure, may change from harmless saprophytes to most virulent parasites, produce remote and secondary inflammatory foci and even septicæmia and ulcerative endocarditis. Pathogenetic organisms, indeed, act either as saprophytes or as parasites, according as they lie on or in the tissues of the body.

It is a common error to suppose that because an organism is found inside some space, cavity, tube or duct of the human body, it lives in the tissues or in the body. In all cavities or spaces in direct communication with the outer world, the same organisms as occur in the outer world may be found. Indeed, unless there exist special preventive measures, those body cavities which are in direct communication with the outside must always contain bacteria. The mouth, the alimentary and respiratory tracts, and the pores of the skin are all in direct communication with—in fact, from a bacteriological point of view, they represent simply—the outer world, and organisms existing outside must often find their way into these body spaces. It is impossible to prevent the entrance of bacteria to the mouth, even if none but sterilised food be taken. The air con-

tains organisms, both such as are capable of producing disease, and such as are harmless. The organisms which find their way into the nose, mouth, and larynx include some undoubtedly pathogenetic forms, as for instance the micro-organisms of pneumonia and suppuration; but though they enter the body, they remain there as a rule without causing any lesions; pathogenetic bacteria are frequently inhaled, but the diseases which they are capable of producing do not ensue. These organisms enter the body, not its tissues, and they thrive in the secretions and on the mucous membranes lining the various body cavities. The resistance of healthy tissues, and the absence of predisposing influence, prevent the pathogenetic organisms present leading anything more than a harmless vegetative existence. The bacillus of tuberculosis in rare cases has been found in the nasal mucous membrane of individuals attending upon consumptives, giving rise, however, to no harmful results, so long as it was outside the tissues on the mucous membrane. But, on the other hand, the micrococcus of pneumonia, which lay harmlessly on the mucous membrane, after a drenching or a chill may assume a virulent character, invade the lung tissues, and in some cases even the circulation.

Action of infection.—Infection may therefore be parasitic or saprophytic, according as the disease-producing organisms live in the tissues or upon the tissues in dead or dying matter. Bacteria manu-facture their toxines wherever they grow, *i.e.* infection is accompanied by intoxication, and it is the latter which produces the really serious changes and symptoms. The results of intoxication may be local or remote, or both. Thus in diphtheria the local changes in and on the tonsils are accompanied by the symptoms of diffusion of the diphtheria poison over distant parts of the body. This remote intoxication again may be general or selective. Thus in hectic or suppurative fever there is a general intoxication, while in tetanus the specific toxine singles out the motor cells of the spinal cord, and in diphtheria the toxine particularly selects the peripheral nerves and their trophic centres. The infection itself may be (*a*) *local* or (*b*) *progressive.* If local, the bacteria remain at the seat of infection, where they may or may not multiply. Examples of local infections are tetanus and diphtheria. If the infection be progressive, it may spread (*a*) by continuity, as for instance in a spreading erysipelas, or it may spread (*b*) by metastasis, which again may be (1) hæmic or (2) lymphatic, *i.e.* the organisms may be carried to distant parts by the blood stream or by the lymph channels. When organisms enter the blood stream, after the manner of emboli, they may be deposited, and so lead to a secondary focus, or they may multiply in the blood and cause a general blood infection, *i.e.* a septicæmia. In many infective diseases, such as typhoid fever, small masses of bacteria may invade a blood vessel, through an ulcerated wall; if they multiply in the blood, the result is a septicæmia, but they may either die or they may be carried away as emboli into the bone marrow or elsewhere, and there produce a secondary focus or a metastatic deposit. The changes produced by an infection are (1) *local* and (2) *general.* The local action of a micro-organism shows itself either as an acute inflammation or as a more chronic process, which may be one of continued inflammation, suppuration, or ulceration, or one of chronic fibrosis (the so-called chronic inflammation). These local changes are produced by the bacteria and their various poisons, and, broadly speaking, the infective organisms and their toxines, unless they kill the tissues outright, cause them to respond by one or other of two re-actions—(*a*) inflammation or (*b*) proliferation of the connective tissue. So far as our present knowledge goes, in man and other warm-blooded

animals, the pathogenetic germs can act in no other direction; they are restricted to the connective tissues as their proper field of action, which they irritate by means of their poisons, it may be into a serous, fibrinous or purulent, a catarrhal or necrotic inflammation, or into a reparative proliferation. The effects which may be observed in epithelial tissues are, whether these be degenerative, desquamative, or even proliferative, secondary to the changes occurring in the connective tissues.

The *local changes* are mainly produced by the non-specific bacterial toxines, the general symptoms of intoxication by absorbed specific poisons, although they (see later) may also produce specific local changes, giving to the local inflammatory or proliferative changes a more or less specific appearance. Thus the local inflammation of diphtheria is specific, as much as it is necrotic and fibrinous, and is accompanied by symptoms and changes partly general and partly specific, which are due to an intoxication by the general and specific toxines of the diphtheria bacillus. In pneumonia the local inflammation is characterised by its croupous nature, and is accompanied by specific symptoms, which are due to the absorption of the specific pneumotoxin, superadded upon those due to intoxication with the general poisonous substances.

The *general action* of infective germs is explained by the absorption of poisonous substances. It is necessary to distinguish between the changes due to intoxication with the general bacterial poisons, and those due to intoxication with specific toxines. The latter produce highly characteristic symptoms, which may be repeated in the experimental animal by infecting it with the specific poison. From diphtheria cultures Martin has obtained poisonous bodies which, inoculated into rabbits, reproduce the ideal picture of diphtheria intoxication, together with the characteristic anatomical lesion; from the organs and blood of children who died with diphtheria the same bodies were separated. The specific toxine of tetanus has also been separated, but up to the present, few others. The general symptoms of infective processes are more or less the same for the different diseases—fever, diarrhœa, wasting, respiratory and cardiac trouble, leucocytosis and inflammation. Centanni has separated a poison (pyrotoxin, closely allied to the proteins) from various bacterial cultures (pneumococci, staphylococci, streptococci, anthrax, typhoid, tetanus, diphtheria, and other bacilli), which both chemically and in its physiological action appears to be identical in all. When injected into the animal, it sets up all the above-mentioned general changes. Bacterial intoxication is evidently not a simple process, and it is necessary to clearly distinguish between the sets of symptoms and changes produced by general poisons and those due to specific toxines.

The *mechanical action* of bacteria in infective processes must not be altogether left out of sight, although it is of less moment than their chemical action. Bacterial emboli may lead to vascular obstruction, or the blood may be so teeming with micro-organisms in septicæmia that the circulation is seriously interfered with. This, however, only occurs during the last days, or it may be hours, of life.

A specific pathogenetic organism is one which, on finding access to the body or its tissues under proper conditions, always produces the same disease, this property not being shared by any other pathogenetic organism. Thus tetanus and diphtheria are examples of truly specific infections, their specificity depending on the fact that the bacilli of diphtheria and tetanus manufacture highly specialised poisons (possessing characteristic physiological action by which they may be recognised), which are not produced by other pathogenetic organisms. There are lesions and appearances which clinically we cannot distinguish from each other, and yet the bacterial flora may vary in individual cases, as for instance infective endocarditis may be caused by pneumococci, staphylococci, or streptococci, and even other organisms. A morbid process which can be caused by several organisms is not a specific lesion, nor is the organism specific for that

lesion. Thus a malignant pustule may be caused by the anthrax bacillus (and this is the rule), but streptococci may also give rise to it. Again, erysipelas is a clinical term used for a disease accompanied by certain local changes and general symptoms. Here the *Streptococcus pyogenes* is usually found, but occasionally other organisms. Furthermore, the streptococcus may produce various lesions, varying from a circumscribed inflammation on the one hand to the most serious septicæmia on the other. The term specific, therefore, can hardly be applied in the present state of our knowledge to any lesion which is purely inflammatory, and is not accompanied by a characteristic form of intoxication. What is clinically one and the same disease may often be caused by a number of organisms, although perhaps one particular organism is more generally found in association with that lesion. It is the same with other irritants; many organic or inorganic poisons produce the same obvious effect when administered to the body, and it is only by a careful chemical examination that the nature of the irritant can be detected. Nitric acid is absolutely different from hydrochloric acid chemically, yet the effects of these two acids on the tissues and the body generally are clinically identical. The physician or surgeon gives a name to a clinical lesion, and the pathologist has to investigate the flora of such lesion. If one and the same organism occurs with the lesion, then it is specific; but if more than one organism is found, then the term specific is no longer applicable. Curative sera used therapeutically act specifically, *i.e.* an antistreptococcus serum is powerless against the pneumococcus. Hence, while dealing with an inflammatory lesion, which clinically may be a cellulitis or a well-defined process, but the bacterial association of which cannot with certainty be predicated, it is necessary to make a bacteriological investigation, and use the antistreptococcus serum only where streptococci are present. In infective diseases, then, the clinical diagnosis must always be supplemented or corrected by bacteriological observation, the methods of the laboratory being carried to the bedside wherever and whenever this is possible. It must be understood that the name which has been given to a disease or a lesion cannot govern or decide its pathology. The exact or objective diagnosis of an infective disease often can be made only by means of a bacterioscopic examination, and just as a physician tests the urine of any renal case for albumin, so he must also search for bacteria in the sputum, urine, blood, or tissues, and apply other methods, such as the serum diagnosis of typhoid fever. Clinical pathology in all its branches—*i.e.* histology, bacteriology, and chemistry, based on good, sound, and quick methods—has now become one of the most important factors in diagnosis and prognosis. No diagnosis of tuberculosis, diphtheria, gonorrhœa, actinomycosis, malaria, typhoid fever, however certain the clinical signs and symptoms, should be made without being supported by a bacterioscopic and microscopic examination; and if there is any doubt at all, as often there must be, which experience and opinion cannot at once remove, an appeal must be made to hard facts, as demonstrated by the platinum needle and the test tube, or on the microscopic slide.

Results of infection.—The pathologist may find that one and the same organism may cause a series of different clinical morbid conditions, or that one and the same clinical condition is produced by a number of organisms. He finds, however, that, disregarding the mode of inoculation and animal resistance, the nature of an infection varies (1) with the dose of germs injected, (2) with their virulence, and (3) with the different forms and species of organisms which enter the body either at the same time or in quick succession.

1. The *number* of pathogenetic bacteria may be so small that the defensive mechanism of the tissues is sufficient to cope with them; a slightly larger dose may produce merely a local inflammatory lesion, a still larger dose a diffuse or progressive lesion, with or without metastatic

deposits, and a further increase a fatal septicæmia. Thus comparatively few staphylococci may lead to a furuncle, which, as the numbers increase, may develop into a boil, carbuncle, cellulitis, accompanied by suppurating glands, pyæmic abscesses, and finally septicæmia. Again, so few streptococci of a given constant virulence may be injected into the rabbit's ear that nothing results, or only a slight local lesion; if more be injected there will be marked erysipelas, and if still more, septicæmia.

2. The *virulence* of an organism may be so powerful, that even small numbers will produce a septicæmia; if it be less virulent, a small number will lead to a diffuse or metastatic lesion; if still further reduced in virulence, merely a local inflammatory lesion; a larger dose, a diffuse inflammation; and a still larger dose, septicæmia; and, lastly, the organism may be so weak that even a large dose will be without effect. These considerations plainly demonstrate how it is that one and the same pathogenetic organism may lead to clinically diverse lesions.

3. At the seat of infection *several pathogenetic organisms may occur together*. Thus in a suppurative focus a mixture of pyogenetic cocci may usually be found; in diphtheria, streptococci frequently accompany the Klebs-Löffler bacillus; whilst in tetanus there is an infection with both tetanus bacilli and pyogenetic cocci. There are mixed infections, if the various organisms have obtained their footing simultaneously. The mixed infection may make its influence felt in three directions—(*a*) the various organisms work independently of one another, as for instance in actinomycosis, where pyogenetic organisms produce ulceration and the actinomyces goes on unmolested; (*b*) one organism may exert an attenuating influence on the other, as may be seen in anthrax, where pyococci weaken and diminish the virulence of the anthrax bacillus; (*c*) the organisms working together in symbiosis, each may exalt the virulence of the other, as in tetanus. These possibilities rest on sound experimental basis, and must be kept in mind during treatment. In diphtheria, death is often due to a septicæmia produced by the streptococcus; and in tuberculosis the ravages of the streptococcus may require as much consideration as the tubercular mischief.

Secondary infection, where a fresh infection is grafted upon the original lesion, must be carefully distinguished from mixed infection. Thus, during the course of an attack of typhoid fever, measles, scarlatina, or variola, inflammatory and suppurative processes, such as erysipelas, abscesses, osteomyelitis, necrosis and endocarditis, often appear, all of which are caused by pyogenetic organisms; again, diphtheria may appear in the course of scarlet fever or measles, or tuberculosis after pneumonia or measles; and yet again a tuberculous process in the lung becomes ulcerative on account of the streptococcus obtaining access to the caseous tissues. In most cases of secondary infection, pyogenetic cocci are the causal agents; they are always about and easily gain access to the already diseased tissues. Secondary infections depend (1) upon the presence in or near the diseased body of pathogenetic organisms; (2) upon the diminished local or general resistance of the tissues already weakened by the primary infection; (3) upon the opening up of fresh paths of infection by the original lesion, which, causing defects and lesions in the vessels, opens a ready portal for the organisms lying in ambush.

PREDISPOSITION.

In the laboratory it is found that some animals fall a ready prey to the activity of certain bacteria, while others are capable of resisting even large doses: some animals are susceptible or predisposed, others are insusceptible or resistant. A predisposition to an infection may be natural, acquired, or inherited. Animals differ greatly in their susceptibility: thus guinea-pigs and mice may be infected even by a few anthrax bacilli, while it requires a larger number for rabbits; for rats a still larger dose; and for dogs exceedingly large doses; hens are altogether refractory. Similarly, animals differ greatly in their susceptibility towards tuberculosis: guinea-pigs are extremely susceptible; mice and dogs are almost refractory. Natural predisposition is therefore a relative quantity —an animal may be said to be susceptible when it is readily infected by any ordinary method of inoculation, without previous preparation and with small or moderate doses of pathogenetic organisms. It must be mentioned that an animal which possesses but little predisposition to an infection with bacteria may yet be extremely sensitive to the action of the poison manufactured by the bacteria. Thus Gamaleia has shown that animals which can resist the living vibrio Metchnikovi, can easily be killed by the toxic products of this vibrio, and certain animals which resist an infection with pure cultures of the tetanus bacillus succumb to the action of their toxine.

Natural predisposition may be the property of a species or of a race : thus all guinea-pigs are susceptible to anthrax or tuberculosis; the dark races are less disposed to yellow fever than are white men. On the other hand, it may be individual, *i.e.* certain members of a species or a race are found to be predisposed to an infection. Age, weight and colour, time and season, and certain unknown factors or idiosyncrasies, all appear to play a part. After a certain age, many infective fevers lose their deadliness. Tuberculosis is commoner in people with certain complexions than with others, but normal man is little predisposed to tuberculosis and leprosy, though it is comparatively easy for him to acquire the disposition, at any rate, to tuberculosis.

It is of the utmost importance to keep in mind that many infective diseases may be staved off by protecting the natural resistance. In the laboratory it is easy to produce an artificial susceptibility. This acquired predisposition may be general or local, according as the resistance of the whole animal or only of some part or tissue is reduced.

General predisposition may be established by conditions which produce merely a general effect on the body—hunger and thirst, fatigue, over-exertion and exhaustion, continued loss of blood and hydræmia, and changes in temperature and in food. Starving pigeons, thirsting hens, and exhausted rats are readily infected with anthrax; anæmic rabbits succumb more readily to the staphylococcus than normal ones; the warmed frog, the cooled hen, and the herbivorous rat all succumb to anthrax. Numerous examples could be cited to prove how easy it is by means of the most general disturbances of conditions which must always exist in poor, overcrowded communities, to break down a natural resistance and establish a predisposition. Certain deadly and distressing infective lesions can be kept at bay only by removing the general conditions which may lead to a predisposition.

Many epidemic diseases, such as cholera, where contagion plays an

unimportant part, invariably play havoc with the poorer classes, living in conditions of filth, hunger, and overcrowding, and the same is probably also true of the plague. Individual resistance is broken down by exhaustion, continued and excessive hard work, and by prolonged poisoning with alcohol. A slight pyogenetic lesion in those debilitated in this manner may assume alarming proportions, and even end fatally. A predisposition thus acquired may again be removed by attending to the causes and improving the general health.

Other more special or well-defined causes of lesions may, however, produce or establish a general predisposition. The immediate effect of a serious operation, such as removal of the spleen, is a lowering of the general resistance ; the presence of sugar in the tissues, as, for instance, in artificial diabetes, renders many animals susceptible to lesions which they can resist in normal conditions, *e.g.* phloridzin feeding renders mice susceptible to glanders. It is a well-known fact that persons suffering from diabetes are prone to pyogenetic lesions, such as boils, carbuncles, and gangrene ; and Minkowsky showed that dogs, after excision of the pancreas, frequently fall victims to suppuration. Clinically it is known that disease of vital organs, such as the liver, kidneys, and heart, predisposes the afflicted to infections, and aggravates the course of an infection : the susceptibility of patients suffering from renal disease to erysipelas and inflammatory lesions is almost proverbial. Certain poisons administered either subcutaneously or by the mouth, or even by inhalation, are capable of breaking down the natural immunity of an animal. Amongst such poisons may be mentioned alcohol, chloral, and chloroform ; further, the hæmolytic poisons, such as hydracetin, phenylhydrazin, pyrogallic acid ; and, thirdly, bacterial poisons. The resistance of an animal against one organism may often be destroyed by infecting it with the chemical products of another microbe, and concurrent inoculations of two organisms will often lead to successful infection. Thus rabbits will succumb to quarter-evil if, simultaneously with the bacilli, the chemical products of the *B. prodigiosus*, *Proteus vulgaris*, or staphylococcus be administered ; and the tetanus bacillus can be rendered extremely pathogenetic for animals capable of resisting the simple infection, by associating it with such common forms as the *B. coli*, the *B. prodigiosus*, and various pyococci. The deleterious effect of poison absorption on the course of an infection has long been recognised. Thus in a case of erysipelas or other pyogenetic lesion, the physician or surgeon begins his treatment by administering a purgative to clear away the poisonous substances which are present in the intestinal tract.

Local predisposition.—It is found that certain organisms, injected into the tissues of an animal, die very shortly without doing any harm. Under ordinary conditions the tissues at the seat of inoculation react well enough with their natural defensive mechanisms to destroy the organisms. In order that they may gain a foothold, the defences of the tissues must be weakened or abolished ; experimentally, this can be done in many ways. Thus, chemical poisons do not necessarily always produce a general predisposition ; their effect may be purely local. For instance, if tetanus spores be injected into the tissues of a guinea-pig with a little lactic acid, tetanus results ; while, without the acid, no harm would have come of the injection. Concurrent inoculation may act in the same way. Hence it appears that the conditions just mentioned may affect the body in two or three different ways :—(*a*) They may weaken the tissues at the seat of infection, so that the organisms have a chance of surviving ; (*b*) they may destroy the general resistance of the body, so that the organisms or their toxines become generally diffused ; or (*c*) a local predisposition having been established, and an opportunity having been given

to the organisms to elaborate their toxines, these gradually undermine the general resistance. It is neither easy nor desirable to keep local and general predisposition too strictly distinct. The natural defences of the tissues may be broken through by contusions, necrosis, or injuries. On inoculating the *Staphylococcus aureus* into the circulation, an osteomyelitis will result more readily if the bone has previously been injured, an infective endocarditis if a cardiac or aortic valve. The injection of tetanus spores will produce fatal lockjaw if, during the injection, the tissues be roughly handled, or the underlying bone be fractured. Here the organisms are merely supplied with the conditions necessary for their survival by the disturbance of the delicately balanced equilibrium. Clinically, this is fully recognised in the case of tuberculosis, pneumonia, acute osteomyelitis, and infective endocarditis; in the last-mentioned disease pre-existing valvular lesions are common. Injuries to the joints in " white swelling," the influence of cold and circulatory disturbances as predisposing causes, are too well established to require further comment. Local lesions, then, may prove great sources of danger, both during infective processes, and also as predisposing causes, and therefore require the fullest consideration and attention of the physician.

It must be remembered that the normal resistance of animals against toxines may also be reduced. Thus guinea-pigs which had been immunised against the vibrio of Massowah (cholera) or the *B. coli* were more susceptible to tetanus toxine than normal animals, and those treated with pneumotoxin were more susceptible to diphtheria toxine. Again, wasted or tuberculous animals succumb more readily to diphtheria intoxication. In this connection it is interesting to note that in many fatal cases of diphtheria active tuberculous changes (broncho-pneumonia or meningitis) or concurrent infections (scarlatina or measles) are found as complications.

Inherited predisposition.—Can an infection be inherited ? Children are frequently born showing signs of infective disease acquired as it is being born or before birth. Thus, instances of ophthalmia neonatorum are common, and congenital tuberculosis, although rare, is by no means unknown; even the typhoid bacillus has been found in the organs of the foetus. The foetus therefore may acquire a microbic disease either *in utero* or during its passage through the vagina into the world. The latter mode of infection cannot possibly be looked upon as hereditary transmission; it is a simple case of contagion. The infected mother infects her child. A little reflection will show that intra-uterine infection is not to be regarded as a true inheritance. The pathogenetic organism is never inherited by the unimpregnated ovum, but *in utero* the ovum or foetus is infected by germs which have passed from a lesion in the maternal tissues, and, after traversing the placental ·filter, have found a suitable soil in the foetal organs. Hence micro-organisms may be transmitted, but they are not inherited. It is found that bacteria do not easily pass through the placental barrier, and that, when they do so, there is generally a lesion in the placenta—a hæmorrhage, *i.e.* a flaw in the filter, or the special organisms, such as tubercle or glanders bacilli, are capable of producing destructive lesions. In the case of susceptible species, the offspring of tuberculous mothers often contain virulent tubercle bacilli in their tissues. These may remain dormant in the tissues for weeks and months, and then produce fatal tuberculosis. Intra-uterine infection through the mother is therefore possible. It may occur in man as well as in animals, but it is an infection, and not an inheritance, and depends on some accident or

other. It is, however, important to remember that, though the offspring of a tuberculous mother may be born with virulent tubercle bacilli in its tissues, it may take months, and even years, for tuberculosis to manifest itself. The predisposition is still absent at birth, and only as it gradually comes on can the dormant bacilli gain the upper hand, and produce their specific effect. Again, the inherited predisposition may be specific, *i.e.* the mother's tissues having been predisposed, the ovum may be similarly predisposed, or this specific predisposition may have been transmitted through the father, in which case frequently phthisis appears in the offspring about the same age as it did in the parent. On the other hand, the inherited predisposition may be general, depending merely on the general weakness and debility of the parents, the infant then being susceptible to infections generally.

As far as the mammalia are concerned, there is no evidence that an ovum is ever infected before or during conception. Careful experiments on guinea-pigs are entirely opposed to such a view. Heredity, then, concerns itself only with predisposition, and never with infection.

CONTAGION.

To the practical physician it is obviously a matter of the utmost importance to know how an infectious disease spreads, *i.e.* whether or no an infected person may prove a source of danger to the community. Formerly, careful, but hardly intelligent or intelligible, distinctions were drawn between infectious and contagious diseases. Now, however, new definitions have been drawn up. The meaning of the term "infective" has been explained at length. A disease is said to be contagious when it is transmissible from the affected to the non-affected, not necessarily to the healthy, because the predisposition which is required for a successful transmission may be, and generally is, a morbid condition. It is better to avoid the term "*contagious*" and to speak of *transmissible infective diseases*.

First, it must be made quite clear that though infective lesions, due to microbes, *may* be transmissible, they are not necessarily so.

Secondly, there are degrees of transmissibility; in some cases a predisposition is required, in others not. Transmission evidently can only take place through contact, but such contact may be direct or indirect. When there is direct contact, then the *materies morbi* must be transferred directly from the diseased person to the victim by touch, inoculation, inosculation, or inhalation; when contact is indirect, then the diseased individual has left the *materies morbi* upon some intermediate object, whence it finds its way into the body of a fresh victim; or, expressing it in symbolic language, when a disease is directly transmissible, it passes from A to B, B', B", etc.; when it is indirectly transmissible, it passes from A through X, X', X", etc., to B, B', B", etc.

Classification.—Infective diseases, then, may be placed in two large groups—(*a*) *transmissible diseases*, and (*b*) *diseases not transmissible*. The latter include relapsing fever and malaria. Certain of the transmissible diseases are produced by obligatory, or almost obligatory, parasitic organisms, *e.g.* gonorrhœa, syphilis, and rabies, although the bacteriology, if such there be, of the two latter diseases is as yet undetermined. Diseases due to such organisms can only be acquired by direct contact; a predisposition is probably unnecessary.

Others of these diseases are due to organisms which possess the faculty of surviving or thriving outside the animal body—facultative saprophytes. With them transmission may be by direct as well as by indirect contact; but the greater their saprophytic faculty, the more important becomes transmission by indirect contact. Amongst the diseases which are due to facultative saprophytes are measles, variola, scarlatina, glanders, tuberculosis, leprosy, diphtheria, plague, and traumatic and pyogenetic infections, though as yet nothing is known of the germs of measles, variola, and scarlatina, or of the saprophytic history of the leprosy bacillus. In some of these diseases, *e.g.* variola and scarlatina, direct contact plays the more important part; in others, such as tuberculosis, where direct and indirect contact play an equally important part, contact segregation is not sufficient to stamp out the disease. In fact, its sufficiency is directly proportional to the saprophytic nature of the disease-producing germ. Thus, although it is for practical purposes sufficient for variola and scarlatina, it is quite insufficient for tuberculosis and diphtheria. Many of these diseases require a predisposition, and it is found that measures may be taken to remove this. The strong and healthy are not harmed by the tubercle bacillus, while for the predisposed tuberculosis is an easily transmissible disease. General hygienic improvement, coupled with vigorous disinfection, has already done much to reduce the mortality from tuberculosis, and in many countries it has stamped out leprosy.

Thirdly, certain diseases are caused by facultative parasites, organisms which are highly saprophytic, such as the bacilli of enteric fever and anthrax, and the vibrio of cholera. Here direct contact may be practically neglected. There is generally an extensive common area of infection in which the disease germs thrive under saprophytic conditions, and whence they infect a large community; these diseases, therefore, are usually epidemic. Here the eradication or disinfection of the common source of infection is of primary importance, and the diseased should not be allowed to continue to disseminate the specific, pathogenetic organisms. Quarantine must be enforced, and all ejecta disinfected. Mere personal segregation, however, without destruction of the source of infection, is absolutely useless.

Lastly, certain infective lesions are due to more or less purely saprophytic organisms, *e.g.* various forms of diarrhœa. Here direct contact need not be taken into consideration, and our attention must be directed to the *fons et origo bacteriæ*, food, or soil, etc.

A little reflection will make it clear upon what points the degree of transmissibility depends—the parasitic or saprophytic nature of the organism in question; its distribution in space; its resistance outside the body; the readiness with which infection is produced, *i.e.* whether or no a predisposition is required, whether any form of inoculation is suitable, or whether special forms are necessary.

An infective disease *is endemic* when it occurs in a given locality, this area never being free from it. In such case—(1) the infective organism must possess a markedly saprophytic nature; (2) there must be suitable external conditions which keep up the source of infection; and (3) the surroundings must be such that, if a predisposition is required, it is always provided. Cholera, for instance, is endemic in Lower Bengal, and leprosy over many parts of India.

Epidemic diseases are those which within a short space of time affect a

large number of individuals; they may visit areas where they were almost unknown, or areas where they are endemic. Infective diseases which are quickly spread by direct contact, especially when a predisposition is hardly necessary, such as variola and scarlatina, are likely to become epidemic; similarly, diseases which are rapidly diffused from a common source of infection, as for instance cholera or enteric fever; and, lastly, diseases which are easily transmitted by indirect contact, such as plague. The epidemic character of a disease depends simply upon the facility and rapidity of infection and transmission, and therefore if in an area where a disease is always at home for some reason or another, conditions arise which render general infection easy, the endemic disease suddenly breaks out with epidemic force.

IMMUNITY.

The converse of predisposition is immunity or insusceptibility; it also may be natural, acquired, or inherited. Natural immunity or resistance is innate, and little is known of its why and wherefore.

In this connection it is necessary to distinguish carefully between an infection and an intoxication caused by a pathogenetic organism. The distinction must not, however, be carried too far; it must be remembered that there is no intoxication without a previous infection, the period passing between the moment of infection and the first symptoms of intoxication being, by the physician, usually called the incubation period. During this period the bacterium which has entered the body or its tissues is actively producing its lesions and its toxines, a certain time, however, elapsing before its effects can be recognised. The incubation period is at an end clinically, either when the lesion is of such size or appearance that it no longer escapes the senses, or when the intoxication has become evident. But, again, just as there is no intoxication without infection, so there is no infection without some intoxication, and it is often the latter which, assuming a recognised type, ends the incubation period. This period is characterised by headache, malaise, and rise of temperature, and eventually the accumulated effect of the toxine absorption gives a temperature chart or a series of symptoms which are satisfactorily diagnosed as the onset. An acute infective fever may be compared to a forced immunisation.

The first inoculation produces no recognisable symptoms in the animal, but as the inoculations are frequently repeated in ever-increasing strength, the animal suffers, often becomes extremely ill, and perchance dies, if an overdose is given. This is a dangerous method, involving loss of animals. It is, however, nature's method, and is best illustrated by the processes observed in typhoid fever. The effects of the early lesions are not recognised, except that there is headache, etc.; as more Peyer's patches and lymph follicles become involved the disease is recognised, and the fever rises and the temperature may become alarmingly high. Each fresh infection of a Peyer's gland may be compared to an inoculation given for the purpose of artificial immunisation, and if it is not carried to excess there comes a period where sufficient immunity is established, the temperature comes down, and, should there be a relapse, the prognosis is good. Much therefore happens during the so-called incubation period; it is the period of careful immunisation which gives the initial immunity. In some infective fevers complete immunity sets in with a crisis, which means that the patient has become proof against the toxine produced by the organisms causing the disease, and that the condition is a pure infection. Often, however, there is a mixed or secondary infection, and then a crisis is out of the question, because, while the patient has become immune with regard to the main or initial infection, he is still susceptible to the other.

In typhoid fever, for instance, when the immunisation against the *B. typhosus* is practically complete, the pyogenetic organisms and the ulcers have still to be reckoned with; hence the suppuration temperature which occurs before the fever subsides.

Natural immunity from infection must be distinguished from natural immunity from intoxication.

The former may be characteristic of the individual, of the species or a variety of that species, of a whole genus or even of a whole class. Cold-blooded animals are, with few exceptions, normally insusceptible to the infections of warm-blooded animals. In warm-blooded animals—birds and mammals—each species or variety must be studied by itself; the natural immunity from various infections seems to have been distributed in an arbitrary manner, although no doubt its establishment is based upon natural and artificial selection, evolution, and heredity. Even amongst the members of a susceptible species immune individuals may be met with (idiosyncrasy).

Natural immunity from intoxication as a rule goes, within certain limits, with immunity from infection, and especially in the case of organisms which are pre-eminently intoxicative, such as the tetanus bacillus, which does its deadly work by sending out its toxine—all the more dangerous because it has a special affinity for the delicate nervous substance of the central nervous system—from the seat of infection. The same may with some reservations be said of the diphtheria bacillus. Hence immunity from diphtheria and tetanus must imply immunity from both infection and intoxication, but mainly from the latter. In some cases animals may resist infections with various organisms, and yet be susceptible to their poisons.

Racial immunity.—The dark races are more resistant to yellow fever and hæmatozoal diseases than others; and it appears also that the native of India enjoys some resistance against typhoid fever. A disease when it first makes its appearance in a race is often extremely deadly in its effects. The existence of individual immunity has long been recognised.

In man natural immunity from intoxication is most important in the case of those pathogenetic bacteria which, under normal conditions, exist in the body, and a natural immunity from infection is most important in the case of those pathogenetic bacteria which enter the body more or less accidentally. Certain definite changes occur in a naturally immune animal subsequent to an inoculation. Should the quantity of bacteria be small, little is noticeable; the organisms are rapidly destroyed; when larger quantities are used, inflammation ending in the annihilation of the microbe without suppuration ensues. Excessive doses may produce suppuration and death even in the immune animal, this being the result of poisoning by the intracellular substances, so that from this point of view it may be said that no animal is absolutely immune. In the immune animal, then, organisms which are pathogenetic to susceptible individuals behave as harmless organisms, and they are incapable of further proliferation, although the poison contained in the cell substance, becoming free with the death of the bacteria, may induce symptoms of intoxication. The immune animal is, however, as a rule able to withstand this poison, reacting fully to doses which would kill susceptible animals. The normal defensive mechanisms of the tissues are sufficient to cope with the bacteria and their poisons, without calling upon the cells to display special chemical activities; in fact, the tissues treat them as ordinary irritants, and destroy them by simple inflammation, accompanied and followed by all the ordinary phenomena of that condition. The bacteria cannot proliferate, because

the inflammatory reaction destroys them as it would destroy irritant necrotic tissue; their poisons can do but little harm, partly because inflammation hinders absorption, favours dilution, and attenuates the poison, which to begin with is but little dangerous to the immune tissues. The tissues and fluids of the body of most animals possess a certain amount of bactericidal and antitoxic power, and this power is greatly increased by the leucocytes and their products; if, therefore, an animal is so constituted that it will react to an infection by reactive and reparative inflammation, there is but little danger of a fatal issue, and in an immune animal an infection produces merely a small local inflammatory change which has no tendency to spread. A certain intensity of irritation is required before the vascular tissues respond by inflammation; if the irritant is too weak, the noxious matter is got rid of by the ordinary normal processes, whether these be regenerative, chemical, phagocytic, or mechanical; and if the number of bacteria and the amount of poison be relatively small, the tissues of the immune animal destroy the invaders at once without making any call upon an inflammatory reaction. The identical process may be seen in susceptible animals inoculated with a subminimal dose. If this be extremely minute, the bacteria are destroyed at once without the slightest inflammatory reaction, a bigger dose will lead to inflammation ending in repair, while the true minimal lethal dose rouses the tissue to an attempt at an inflammatory resistance, which is, however, unsuccessful. It is obvious, then, that an animal is immune when its tissues are so constituted that even comparatively large doses of bacterial poisons have no further action beyond stimulating them to immediate or inflammatory repair; and the degree of resistance is measured by the maximum dose of bacterial poison to which the animal can respond with reparative reaction.

IMMUNISATION.

When a rabbit (which is an animal strongly predisposed to anthrax) is inoculated subcutaneously, intravenously, or intraperitoneally, with comparatively few anthrax bacilli, it succumbs to anthrax septicæmia. Now, if it be treated in such a manner that a similar quantity, and even a larger quantity of the anthrax virus is borne without serious harm, it is said to have been immunised or protected. Immunity cannot be understood without a sound knowledge of the methods of immunisation, which may be either non-specific or specific.

Non-specific immunisation.—An animal may be protected against an infection with a given organism by the use of *bacteria belonging to entirely different species or genera.* Thus, as shown by Klein and others, if a guinea-pig be inoculated intraperitoneally with the *B. typhi abdominalis,* the animal becomes immune against intraperitoneal injections of totally different bacteria. Again, previous treatment with the streptococcus of erysipelas (*Streptococcus pyogenes*), or sterilised culture of *B. pyocyaneus,* induces in certain animals an immunity against anthrax. In such cases the immunity is most marked if the inoculation be made in the situation at which the immunising injection has been administered. This process of immunisation is probably a chemical one, because, instead of the living cultures used for the purpose of immunisation, sterilised cultures, *i.e.* their chemical products, may be used. Again, the immunity produced is merely temporary, disappearing in small animals in one to four weeks. A specific immunity against cholera, produced by previous injections of cholera vibrios or their products, lasts for months; a vicarious immunity produced by previous injections of the *B. pyocyaneus,* for instance, lasts only two to three weeks. Thirdly, a specific immunity is general,

i.e. after the animal has been immunised it does not matter where the test dose is injected, but in a vicarious immunity the best results are always obtained, when the test dose is injected in the same situation as the immunising dose.

Pfeiffer, Issaeff, and others have shown that instead of living or dead cultures of micro-organisms, such solutions as broth, urine, saline, or other chemical solutions, when injected into the peritoneal cavity of an animal, set up a peritoneal immunity identical with that just described. This appears to favour the theory that the process is purely chemical. Others have used extracts of tissues or cells, as for instance thymus and testicular extracts, yeast nuclein, normal blood serum of animals, spleen extract, spermin, etc., all of which, to a certain degree, inhibit bacterial growth, and it was imagined that they exerted an antiseptic or disinfectant action. Here again comparatively large quantities are necessary, and the immunity is merely temporary and local. Normal blood serum, in quantities altogether insufficient to act as a disinfectant, injected into the peritoneal cavity of a guinea-pig, will protect it against a choleraic intra-peritoneal infection. Hence the immunising action is not directly bactericidal.

If an animal be immunised against the cholera vibrio by repeated injections with this organism, its serum gradually acquires a strong protective action, *i.e.*, a small quantity inoculated into an unprotected animal will render it immune against a lethal dose of choleraic material. Supposing that 1 c.c. of serum of a normal animal, when injected into the peritoneal cavity of a guinea-pig, would protect this animal against the lethal dose of cholera vibrios, a fraction of 1 c.c. (say $\frac{1}{10}$ c.c.) of serum from the immunised animal will produce the same effect. Now the normal serum would also have protected a guniea-pig against intra-peritoneal injections of other organisms, *e.g.* the *B. coli.* But although $\frac{1}{10}$ c.c. of the serum from the immunised animal is sufficient to im-munise against the lethal dose of cholera vibrios, 1 c.c. of this serum is required to protect against the *B. coli.* The effect produced by immuni-sation with bacteria (or their products) then is specific. Again, if a guinea-pig be injected intraperitoneally several times with *B. pyocyaneus*, it would be immune from the effects of intraperitoneal injection of *B. prodigiosus.* Its serum now has a specific action against *B. pyocyaneus*, but hardly any against the *B. prodigiosus.* This shows that although the injection of one organism may produce a marked local immunity against another organism, the general effect on the tissues is specific. The most noteworthy local changes which occur during the process of non-specific immunisation is a local leucocytosis, accompanied, however, by a slight general hæmic leucocytosis, indicating a slight general effect. Fever and local inflammation, which are both frequently produced, are reactions of the utmost importance.

All the different processes mentioned so far, do not act as directly germicidal; they produce changes, most marked at the seat of inoculation, but not absent elsewhere, and these changes are followed by a temporary diminution of the predisposition towards infections generally. It has been shown experimentally that a general immunity may be produced in an animal by injecting it with drugs, enzymes, or albuminous substances which produce a marked hæmic leucocytosis; and it has actually been recommended that pilocarpine injections, which produce a considerable increase in the number of white corpuscles in the blood, should be used therapeutically. Further, it is generally recognised that in many infective fevers the number of leucocytes in the blood is, under certain conditions, a good index as to the progress of the patient towards recovery, *i.e.* towards immunity. Thus,

with a more or less severe infection, if there is marked leucocytosis, the reaction is good, and prognosis is favourable, while if leucocytosis is absent the reaction is weak, and the chance of recovery is less. Probably other changes, as yet unrecognisable, take place in the body, under the conditions now under discussion, and along with leucocytosis.

Non-specific immunity, the result of a previous infection, has as yet not been observed in man; on the contrary, it is a demonstrable fact that during convalescence from one infective fever, an individual may acquire others which run their clinical course undisturbed; and Dr. Caiger says "the symptoms of one disease are neither delayed in their appearance, nor mitigated in their severity, by the presence of another, but the characteristics of each are for the most part well defined, and in some instances even exaggerated." It is, however, not the relation between convalescence and fresh infection which is of importance, but that between complete recovery and fresh infection. Animal experiments show that all our inoculations in the study of immunity must be made when there has been a complete *restitutio ad integrum*; indeed, during convalescence animals are often more highly susceptible to fresh infections.

The treatment of peritoneal tuberculosis by mere drainage is well known to all, and there can be no reasonable doubt that the success of this procedure depends (as pointed out by Durham) upon this principle of non-specific protection, which raises the resistance and destructive powers of the peritoneal membrane.

A general non-specific immunity may further be established by the *administration of chemical substances before infection.* Thus, von Fodor and others have shown that in many animals, by raising the alkalinity of the blood, a temporary protection may be effected, and it is claimed that there is a distinct relation between the degree of alkalinity of the blood of animals before and after recovery, and their susceptibility.

A local inflammation will often procure a local non-specific protection, the degree of the latter varying directly with the amount of leucocytosis produced at the seat of inflammation. This may account for the immunising action of the various substances mentioned above, local inflammatory lesions progressing favourably towards repair, protecting against infection by virtue of the leucocytic and other exudative changes. Thus it is well known that granulating wounds are only with difficulty infected. Cartwright Wood and Cobbett have shown that a simultaneous or previous inflammation may often produce a temporary, more or less local, immunity to erysipelas, which is non-specific in character. On the other hand, if leucocytosis be absent, as for instance in an œdematous inflammation, there is, instead of protection, often increased susceptibility.

The good effect of inflammation has also been taken advantage of clinically, for the purpose of curing chronic infections of a milder type, *i.e.* for the purpose of establishing a local immunity, as in the tuberculin treatment. On injecting a patient suffering from lupus with tuberculin, a local inflammatory reaction appears around the lupoid area, accompanied by fever and a general hæmic leucocytosis. This local inflammation cannot as yet be explained, but cure or local immunity undoubtedly follows its appearance in certain cases. Cantharidin, albumoses, peptones, and bacterial extracts, all produce fever or hæmic leucocytosis, affording further illustration of the relation between leucocytes and general immunity. Further, the good effect of an acute inflammation upon a chronic infective process may be instanced in connection with the use of blisters, fomentations, and poultices, injections and applications of nitrate of silver or sulphate of copper, which, awakening a slumbering process into acuteness, have cured many a lingering affection. It has, as yet, not been proved that the rise

of the body temperature *per se* is sufficient to set up either general or local non-specific immunity; indeed, apart from the leucocytic changes in the blood during an infective fever, the rise of temperature and the increased metabolic activity may be actually harmful.

Non-specific immunity against toxines can also be produced by injections of different fluids into the peritoneal cavity. Thus Calmette has shown that the previous inoculation of a guinea-pig with broth, or different kinds of serum, raises the resistance of the peritoneum against toxines.

The general resistance of a tissue against bacteria or toxines may be artificially raised by prophylactic injections of various solutions; these appearing to react by producing a general or local leucocytosis, or, as in the case of alkalies, by altering the chemistry of the blood. That this latter point must not be forgotten, is clear from the experiments of Freund and Gross, who showed that the injection of substances capable of preventing coagulation will render animals proof against diphtheria intoxication.

Specific immunisation.—By specific immunisation is understood— (1) a treatment with a given living micro-organism, or its chemical products, derived either from the dead bodies of the micro-organism or held in solution by the culture fluid; or (2) a treatment with chemical substances derived from and held in solution by the blood or other fluid of an animal treated as in (1). In either case the result of the treatment must be an immunity from an infection with that micro-organism, or an intoxication with its products; an immunity which is specific in this sense, that the resistance against the organism in question, or its toxines, has been raised out of all proportion to what would have been brought about had the treatment been general. In the first case the micro-organisms or their products are administered to the animal, and the latter passes through an attack of the infection or intoxication, and on recovery from an illness of some duration has acquired a marked protection, or immunity of specific character. In the other case, a portion of the immunity acquired by one animal is transferred to a normal and susceptible animal; here the latter suffers no illness, it merely accepts the protection for which the other animal had to struggle. It is evident that there is an essential difference between the two methods of immunisation; and since, in the one case, the tissues must fight and react visibly, but in the other are apparently merely passive recipients, the first mode of treatment is called active immunisation, the other passive immunisation.

1. **Active immunisation.**—An animal may be rendered either highly *infection proof,* or highly *toxine proof;* but it must be remembered that an animal which has been specially immunised against living virus possesses also a certain amount of toxine immunity, and *vice versâ.*

(*a*) *Active immunisation against living virus* in the laboratory may be brought about—(1) by the use of attenuated virus; (2) by inoculation with sublethal doses of bacteria; (3) by changing the portal of infection; (4) by injecting the chemical products of the virus. There are, of course, other methods of active immunisation; these four, however, illustrate the principle underlying artificial immunity.

(1) *Attenuated virus.*—Pasteur showed that an attenuated virus produces an immunity against a stronger one, and pointed out that an immunity against an infection follows upon the administration of attenuated micro-organisms. The attenuation must be carried only so far that

the organisms still remain capable of growing at the seat of inoculation, and of producing a local lesion. The animal passing through a mild form of the disease is, after complete recovery, able to resist a reasonable dose of strong virus. This method is employed to obtain protection against anthrax, fowl cholera, swine erysipelas, and rabies. It is evident that, having once got the animal to withstand a dose of strong virus, it may be accustomed gradually to bear larger doses by repeating the injections, and at the same time gradually raising the virulence of the bacterial culture used. Beginning, then, with attenuated virus, in order to awaken the defensive powers of the tissues, and continuing with stronger and with increasing doses of it, an extraordinary immunity from artificial infection may be obtained; an immunity which is specific in this sense, that, although the treatment has temporarily somewhat raised the general resistance of the animal, the protection against the virus used for the purpose of immunisation is considerable and enduring, proportionate to the doses used, and the virulence of the organisms employed.

Attenuation of micro-organisms may be produced in many ways, of which the following may be mentioned. By—(a) growing them at a raised temperature (anthrax at 42° C.); (b) exposing them to sunlight (B. tuberculosis); (c) desiccation (bacillus of quarter evil); (d) electrolysis; (e) exposing them to a raised atmospheric pressure; (f) bringing them into contact with free oxygen; (g) adding antiseptics to the cultures; (h) growing them for a longer or shorter period in test-tubes; (i) by concurrently inoculating another organism; (k) by passing the organism through the animal body; and (l) by attenuating them *in vivo* by simultaneously injecting chemical substances, such as normal serum and antiseptics, which either awaken the resisting powers of the tissues or diminish the virulence of the organisms. In attempting to produce an artificial specific immunity, too much should not be demanded from the tissues. They can counteract a certain dose of bacteria, which naturally varies inversely with the virulence. An excessive dose of attenuated organisms will kill as certainly as a small dose of virulent ones, unless attenuation be carried so far that the organisms have become absolutely powerless. As the tissues are always capable of accounting for a certain number of bacteria, an active immunity from infection may be obtained even by *beginning with sublethal doses of virulent organisms.*

(2) *Sublethal doses.*—It is easy to immunise animals against typhoid, cholera, or pyocyaneus infection, by using a smaller dose than the minimal lethal one; such doses, however, must be sufficient to cause local changes. A strong immunity may be quickly produced by giving repeated minute injections. Thus, by inoculating a guinea-pig intraperitoneally every two hours with $\frac{1}{20}$ to $\frac{1}{10}$ the lethal dose of typhoid bacilli, an immunity is produced against forty to fifty times the lethal dose within twenty-four hours; this is enduring and specific in the sense explained above, *i.e.*, although the resistance against the typhoid bacillus is raised forty or fifty-fold, that against other organisms is only slightly raised.

(3) *Change of portals of infection.*—Organisms often vary as to the effect they produce in the body, according as the injection has taken place subcutaneously, intraperitoneally, or intravenously, etc. Instead of using attenuated virus or a minute dose, an inoculation of a larger dose may be given in the least harmful situation. An animal can bear a larger dose of B. pyocyaneus subcutaneously than intraperitoneally or intravenously, a larger dose of typhoid bacilli intravenously than intraperitoneally, a larger dose of diphtheria bacilli intraperitoneally than subcutaneously.

For the three experimental methods of active immunisation above described, analogous examples may be found in medicine. Thus, it is a well-known fact that recovery from an infective disease conveys an immunity of shorter or longer duration. This natural process of immunisation may be compared to protection by sublethal doses. Vaccination against variola in all probability affords an instance of immunisation by attenuated virus, and the old process of variolisation illustrates the method of protection by change of portal, as also does Haffkine's method of anticholera vaccination.

(4) *Chemical products of the bacteria.*—Instead of using living virus for the purpose of immunisation, either the dead bodies of the bacteria themselves, or the substances which are held in solution by the culture fluid, may be employed. It is important to distinguish between immunisation by the chemical substances contained in the bacterial bodies, and immunisation by the chemical substances found outside the bacterial bodies. As far as the outward result is concerned, an immunity against infection is produced whichever chemical substance is used; but although an animal immunised with extracellular chemical substances acquires specific protection, both against the living bacteria and those extracellular poisons, an animal immunised with living or dead bacteria has but little, or at any rate considerably less, protection against these poisons, in spite of its acquired immunity from an infection with the living bacteria themselves.

(*b*) *Active immunisation against toxines* is carried out either by repeated inoculations of weak toxine, or of minute sublethal doses of strong toxine. It is possible to establish a toxine immunity, not only in the case of bacterial poisons, but also in the case of certain animal poisons, and some derived from the higher plants. Amongst the animal poisons are snake venom and scorpion poison; amongst those of the higher plants, abrin, ricin, and robin. These toxines are chemically, apparently, closely related to those of bacterial origin; they all belong to the group of albuminoid bodies and are not alkaloidal in nature. It is possible to establish a tolerance against alkaloids and poisons of simpler constitution (such as inorganic poisons, arsenic, etc.). Tolerance of a poison is, however, different from toxine immunity; it is acquired, and progresses, slowly (while an immunity, although slowly acquired, progresses more quickly), and is accompanied by changes in the body leading to the production of an antitoxic serum. The fact that only poisons belonging to the group of toxines or enzymes can be used for the purpose of obtaining an antitoxic serum is important, because it shows that in this respect there must be some relation between the chemical constitution and the physiological action. The serum of an animal accustomed to large doses of arsenic, opium, or strychnine, does not become antitoxic.

In the case of tetanus and diphtheria, it is possible to obtain a high degree of toxine immunity by using minute doses of toxine, slowly and gradually increased, or by first injecting subcutaneously toxine attenuated by the addition of iodine solution. An initial toxine immunity having once been produced, it can be readily raised by repeating and increasing the doses of pure or undiluted toxine. In some cases gastric administration will produce an active immunity, as in the case of abrin and ricin, and it is said also of snake venom, tetanus, and diphtheria.

If an animal be immunised with bacterial toxines or with bacteria which kill by intoxication, it becomes proof (*a*) against the corresponding infection, as well as (*b*) against the intoxication; but, on the other hand, animals immunised with

living bacteria, which generally kill by septicæmia, become proof only against the infection. Thus diphtheria or tetanus bacilli will produce both a toxine and an infection immunity ; diphtheria toxine, tetanus toxine, pyocyaneus toxine will all do the same ; but the living culture of *B. pyocyaneus, B. typhosus, B. choleræ,* etc., will produce protection from the living cultures only ; and even in the first case it has been found, for diphtheria at least, that if living cultures only be used, the infection immunity is greater than the toxine immunity, whilst if toxines are used the conditions are reversed.

Again, although a single dose of toxine may suffice to obtain an infection immunity, it may, and generally does, take many doses to produce even an initial toxine immunity ; it is therefore much easier to establish a marked resistance against the living organism than against their toxines,—a point worth considering in the treatment of infective diseases. It is interesting to note that if an animal be immunised by means of increasing doses of living cholera or typhoid cultures, a point is at last reached at which a further injection of living culture kills the animal. This appears to be because the poison contained in the bacterial cells, dissolved and destroyed in the body of the bacteria immune animal, is liberated, a poison against which the animal has not been immunised.

2. **Passive immunisation.**—We must now speak of passive immunisation, which is based upon this fundamental law : *The serum of a specifically immunised animal, when injected into another animal, confers upon the latter an immunity from infection with the organisms against which the first animal had been protected.* (1) The action of this serum is specific, with a few limitations to be stated shortly. (2) The immunising value varies directly with the degree of antitoxine present in the serum given. (3) The blood of a naturally immune animal does not possess the power of an artificially immunised animal.

(*a*) *Passive immunisation against infection.*—It is quite immaterial by what method an animal is immunised against an infection, *i.e.* whether dead or living bacteria or their extracellular products be used ; so long as the animal is rendered highly bacteria proof, its serum will also acquire strongly immunising powers. There is, however, a difference. Immunisation with dead or living bacteria produces an antibacterial serum ; immunisation with extracellular bacterial toxines, one which is both antitoxic and antibacterial.

(1) *The specificity in action of the serum derived from immunised animals.*—In the serum from an animal highly immunised against cholera vibrios, the serum has a marvellous preventive action against an infection with cholera vibrios, but it must be confessed that it also has a marked action upon infections with other organisms. Has it then no specificity ? Certainly it has ; for even normal serum has a general restraining influence which is not affected by the process of specific immunisation, which, however, greatly increases the specific action of the serum. A single example will make this clear. 0·2 c.c. of serum of a normal goat is capable, as shown by Pfeiffer, of counteracting an infection with 2 mgrms. of virulent vibrios, and similarly against an infection with 2 mgrms. of virulent typhoid bacilli. After the goat has been immunised against typhoid, 0·005 c.c. is sufficient to counteract 2 mgrms. of virulent typhoid bacilli while it still requires 0·2 c.c. to inhibit 2 mgrms. of cholera vibrios ; and conversely, after the goat has been immunised against cholera, 0·002 c.c. suffices to neutralise 2 mgrms. of cholera vibrios, while it still requires 0·2 c.c. to counteract 2 mgrms. of typhoid cultures. It follows, therefore, that the newly acquired

antibacterial substance is different from the general antibacterial substance, and is truly specific.

(2) *The immunising value of the antibacterial serum varies with the degree of immunity produced.*—A single injection with bacterial toxine is often capable of establishing an initial immunity from an infection with the lethal dose of living bacteria, and it has been shown that this immunity appears critically, *i.e.*, it appears more or less suddenly after one, two, or three days, or even a longer interval. Again, the appearance of this initial immunity is not directly proportional to the amount of toxine used, *i.e.* some animals react to smaller doses than others. Immunity appears, therefore, after a reaction, which is sometimes short, sometimes prolonged, which may be called forth by smaller or larger doses of toxine. During the initial stage of immunity, the serum of the animal has but little if any antibacterial power; to obtain this it is necessary to raise the initial immunity, so that the animal can withstand many times the lethal dose. To produce the initial immunity the animal must be made to react, the symptoms and signs of reaction being local inflammatory changes, fever, local and hæmic leucocytosis; and to raise the initial immunity it is necessary to increase the dose, so that the animal reacts to each inoculation, because, as the animal becomes immune its sensitiveness becomes diminished. If, for instance, an animal be immunised with a sublethal dose of toxine, and this same dose be given for weeks and months, the animal acquires an initial immunity against the lethal dose, but never against many times that dose. If, however, when the initial immunity has been obtained, a larger dose be injected, and then, when the reaction has entirely subsided, a larger dose, and so on, the animal eventually acquires an immunity against many times the lethal dose, and antibacterial serum can be obtained.

An antibacterial serum may be obtained in two ways—(1) dead or living bacteria alone may be injected in ever-increasing doses; or (2) increasing doses of the extracellular toxines may be used. There is this difference in the result: the first method yields only an antibacterial serum, while the latter method yields a serum which is both antibacterial and antitoxic. In either case, the immunity of the animal becomes raised, and the power of the serum for a time becomes more marked, so that, while to begin with perhaps 1 c.c. of serum was required to counteract the single lethal dose, later on 0·005 c.c. will be found sufficient.

(3) *The blood of a naturally immune animal does not possess the power of that derived from an artificially immunised animal.*—An active immunity can only be obtained slowly, and requires a reaction on the part of the animal which is being treated, and it has been found that an animal which is very sensitive and gives the highest reaction will also yield the most potent antibacterial serum. Therefore it is not surprising that the serum of naturally immune animals has no action beyond that general action against infection which belongs to all forms of serum, though by giving a naturally immune animal an injection of the bacteria which are harmless to its tissues, a specific antibacterial serum of weak potency may be obtained: this clearly proves the essential difference between the two kinds of serum. Again, an injection of immunising serum into a naturally immune animal will impart to the serum of this animal the new and specific properties. All these considerations are important, because they show that during immunisation special chemical changes take place which produce conditions differing essentially from pre-existing ones. Artificial specific immunity cannot be a mere elaboration of the natural general immunity.

Active immunisation is a process which requires time and patience, and a marked reaction on the part of the animal undergoing the process; passive immunisation, on the other hand, is quick and sudden, and, while working with low multiples of the lethal dose, is proportional to the amount of serum injected. It is, however, not possible by using the serum of an immunised animal to transfer to another animal the same amount of resistance which the giver of the serum has slowly and laboriously acquired. The passive immunity is at its height almost immediately after the injection of the serum, and then gradually diminishes; the active immunity is more lasting.

(*b*) *Passive immunisation against toxines.*—Just as it is possible to produce a passive immunity against infections, so also in regard to intoxications. An animal rendered highly toxine proof yields a serum which will protect a susceptible animal. (1) The action of the serum is specific; (2) its immunising value depends upon the degree of immunity acquired;[1] and (3) naturally immune animals do not possess a serum of the same power as that of an artificially immunised animal.

If antitoxic serum be mixed with toxine in certain proportions, the mixture injected into an animal remains harmless—the poison has been neutralised; if less serum be used, the neutralisation is partial, and the animal succumbs or recovers after a prolonged illness. The serum may be injected into the animal before, together with, or after the poison, and in no case does evil ensue. The neutralisation is not a merely chemical one, for the amount of antitoxic serum required for a given dose of serum varies with the susceptibility of the animal; thus a mixture of toxine and antitoxine may be harmless for one animal, whilst it is still fatal for a more susceptible animal. Tetanus toxine with antitoxine, mixed in such proportions as to be no longer injurious to 1 kilo. of white mice, is still toxic for 1 kilo. of guinea-pigs. In the process of immunisation, then, the condition of the cells of the animal which receives the serum is of the utmost importance, and if it requires a certain amount of diphtheria antitoxine to neutralise the lethal dose of diphtheria toxine for a healthy guinea-pig, a larger dose of antitoxine is required for a starved or weakened guinea-pig. The immunity is produced immediately, and in the healthy the antitoxic serum is as harmless as the antibacterial, or as the normal serum.

The antitoxic properties are acquired only some time after immunisation has been begun, and they remain at their height only so long as immunisation is continued, and may finally vanish, although the animal may still possess considerable protection, immunity continuing without a concomitant antitoxic power of the serum. During the process of immunisation it is found that immediately after each injection the antitoxic value falls slightly, after which it rises to a higher level than it had previously reached; whilst, after bleeding an animal to obtain its antitoxine, the loss is almost at once made good by the cells of the body, showing that the production of antitoxine depends on cellular activity.

To obtain an antitoxic serum, toxine in ever-increasing quantities, and to produce a high antitoxic potency, strong toxines, must be used. The antitoxic and antibacterial substances, although they may coexist, are not the same. Thus, in the case of immunisation with the *B. pyocyaneus* or its toxine, it has been shown by Wassermann that after immunisation with increasing doses of toxine, the serum contains both antibacterial and antitoxic powers; and that, if at a given moment the immunisation be continued with living cultures, the antibacterial power rises, while the antitoxic value falls, and may be reduced to zero; and, finally, that after immunisation with living cultures, the serum may be strongly

[1] This does not hold good in the same sense or degree that it does in the cases of immunity against infectious.

antibacterial and yet possess no antitoxic powers; but if it possesses antitoxic powers, it always possesses also antibacterial powers. With a serum which is both antitoxic and antibacterial, it is much more difficult to protect against a lethal dose of poison than against a lethal dose of culture. Roughly calculated, it requires 100 times as much serum to counteract the toxine as is required by the virus.

Specificity of antitoxic serum.—It has been shown, especially by Calmette, that the serum of an animal immunised by repeated and ever-increasing doses of one snake venom has a preventive action upon the poison of other snakes, and even upon the poison of a scorpion. This statement, although challenged with regard to the poison of Russell's viper, is in the main apparently true, because of the close chemical and physiological relation between the different venoms. Just as the cholera serum will protect against all the varieties of cholera vibrios, so the antivenomous serum derived from a cobra-poison proof animal may be expected to counteract all allied varieties of poison.

A feeble antitoxic action may be discovered in the serum of many normal animals, in one case against snake poison, in another against diphtheria toxine, and so forth, but there is no correlation between natural immunity and this power of the serum. Again, Calmette has shown that an animal vaccinated with and against abrin, yields a serum which has some effect on diphtheria toxine and ricin, although the last observation is strenuously denied by Ehrlich. Certain experiments tend to show that the serum of animals immunised against certain poisons is capable of acting against other poisons, but from these it cannot be concluded that antitoxic serum is not specific, because as yet there is no serum capable of counteracting a number of poisons, or even of neutralising two different poisons with the same energy. It appears that in some cases, by the process of immunisation, the serum is developed in one particular direction, and occasionally also slightly in another, or it may be in several other directions. But whenever a real vicarious action of an antitoxic serum upon another heterologous toxine is developed, as for instance in the case of snake venoms, it may be accepted that there is some close chemical and physiological relation between the toxines, an assumption ably defended by Ehrlich. The physician, for the present at any rate, must regulate his treatment in accordance with this faith in the specific action of antitoxines.

THEORY OF IMMUNITY.

Natural immunity.—What factors co-operate to render the tissues so resistant that they either remain unaffected by pathogenetic bacteria and their toxines, or react against them with their normal methods of defence? This resistance is not due to any of the following factors—(1) absence of nutrient material in the tissues; (2) unsuitable temperature; or (3) reaction of the blood and lymph. It can be shown, however, that the animal body possesses in its fluids antibacterial substances, for, if absolutely harmless bacilli be injected, they die rapidly, even when protected from the direct action of the cells; and further, the presence of these substances in the blood serum and different exudations has been clearly demonstrated by test-tube experiments. There is, however, no absolute correlation between the antibacterial action of serum, as measured by test-tube reactions, and natural immunity; this latter, therefore, cannot depend upon this property of the body fluids; still it is important to keep in mind that under certain conditions these fluids may display this destructive power over many forms of bacteria. Often this display does not take place until the animal has been infected. Thus it has been shown that the blood of the dog, an animal immune from anthrax, possesses *in vitro* no antibacterial power against the *B. anthracis*, until the animal has been inoculated with this bacillus; and Pfeiffer and Issaeff have shown that the injection of guinea-pig's serum into a guinea-pig

raises the bactericidal power of the latter. These antibacterial substances, there-fore, can (a) partly exist in the serum, and (b) partly are poured into it as the result of some reaction, and probably have a common origin, being natural products of the leucocytes, as a direct correlation has been clearly demonstrated between the number of white blood corpuscles present in blood serum or exudation, and this bactericidal power. In inflammation, leucocytic infiltration occurs *in situ*, and there is generally a copious hæmic leucocytosis; hence the amount of bacteri-cidal substances both *in situ* and in the circulation must be considerably increased, and in the susceptible animal the infecting bacteria are promptly destroyed, if they are so balanced against the tissues as to irritate them to reparative inflam-mation; leucocytes appear to supply additional antibacterial substances; the latter destroy the micro-organisms, and their intracellular poisons attract still more leuco-cytes by a process of chemiotaxis. Phagocytosis will also occur, as it does in every form of reparative inflammation, but only when the fight is practically over. Useful it is, and no doubt it assists in the struggle, but it is not the cause of immunity any more than it is the ruling principle of inflammation. It is an observation which can be easily made, that bacteria can be inhibited and destroyed *en masse* without the intervention of phagocytosis. Finally, it must be mentioned that antitoxic substances are found in and given out by the leucocytes, so that, so far as these cells are concerned, the foundation of natural immunity is fairly firm; it must be understood, however, that exclusive importance must not be attached to this one class of cells; there may be other cells, other organs in which bacteri-cidal or antitoxic substances are secreted or produced—the liver, for instance. The naturally immune body reacts to a bacterial invasion, just as it would to any form of irritation, by means of its natural defensive mechanisms.

Attempts have been made by several observers to separate the antibacterial substances in the serum. Büchner found that heating to 55–60° C. for a half to one hour, and the addition of water, destroy them, that the addition of sodium sulphate increases their action and resistance, and that 40 per cent. sodium sulphate precipi-tates them. He gave them the name of atoxines, and classifies them among the albuminoid substances. Others have shown that nuclein and nucleinic acid have markedly bactericidal and immunising properties. All agree that the leucocytes are one of the main sources of these substances, whether set free by secretion or by the death of the corpuscles (Metchnikoff's phagolysis).

Acquired immunity.—(a) *Non-specific immunity.*—Non-specific acquired immunity may be explained by assuming that the substances used for immunisa-tion react on the tissues, inciting them to inflammation, which is accompanied by a local infiltration of leucocytes, and a general hæmic leucocytosis. This results in a production of general antibacterial and antitoxic substances, which evidently will be present in greater abundance at the site of the inflammation than elsewhere; hence the non-specific immunity is always most evident locally, *i.e.* where the immunising injection was administered. This is readily understood after what has gone before, but it must not be forgotten that other factors besides the leuco-cytes may play a part. Moreover, there are various forms of leucocytes, and therefore various forms of leucocytosis; and it appears that from the different types of leucocytes, different substances are obtainable: thus the atoxines of Büchner are traced to the granular leucocytes, while from the lymphocytes anti-toxic substances (nucleo-histon) have been prepared. A non-specific artificial immunity is of short duration, because the increase of the general or normal anti-bacterial and antitoxic substances is temporary, and the latter are soon used up and eventually excreted; they have been found in the urine of animals during and after recovery from artificially produced fever.

(b) *Specific active immunity.*—If an animal be immunised by means of sub-cutaneous injections with a toxine—(a) its resistance both against other toxines and bacteria as a whole is slightly, mainly locally, and temporarily raised; (b) its specific resistance against the bacterium which yielded the original toxine is con-siderably, uniformly all over the body, and more enduringly raised; and (c) its

specific resistance against the toxine itself is raised still more, and equally, uniformly, and enduringly. This may be explained by assuming—(1) that the injections, by producing repeated inflammatory reactions, cause an increase of the general or normal antibacterial and antitoxic substance, more marked locally than elsewhere; (2) that the toxine, repeatedly and in steadily growing doses injected into the tissues, produces chemical changes in them of a more lasting nature, and uniformly distributed over the body; these result in the formation of specific antibacterial and antitoxic substances, the latter being present in larger quantities. The slight non-specific general immunity soon disappears, and with it the amount of general antibacterial and antitoxic substances is brought to its normal level; but the specific immunity from infection and intoxication continues, and during the greater period of its continuance the blood or serum displays both specific antibacterial and antitoxic powers. Eventually both may be lost while the immunity from infection and intoxication still persists. These specific substances are newly acquired, and are not evolved from those normally existing, because the latter, except immediately after an immunising injection, do not alter in the least. How they are acquired and whence they come is not known. They are essentially different from the normal substances (Büchner's atoxines), for they bear heating at 60°; and when injected into a normal animal, they produce a specific passive immunity, while with normal serum only a very slight temporary immunity can be produced. The specific antibacterial and antitoxic powers are gradually developed and distributed. Centanni found that at the end of the antirabic vaccination the blood displays some immunising action, while in the spinal cord this is absent; after two weeks, blood and cord possess it to the same degree; and after a further four weeks the cord alone is active, while in the liver, kidneys, and spleen no immunising substances are found at any period. From all this it follows that the specific antibacterial and antitoxic substances are products of certain unknown reactions in the living body, and are not merely altered toxines. As Ehrlich pointed out, they are not a new creation of strange atomic groups, but a reconstruction of existing ones, comparable to a process of fermentation. Certain affinities exist between toxine and certain cell constituents; thus tetano-toxine is taken up and held with avidity by the motor ganglion cells, so that the latter must contain atom groups possessing a special and specific affinity for this toxine. A minimal quantity of poison, at the commencement of immunisation, at once combines with the atom group, which has an affinity for it; and the cell immediately, according to the law of repair, forms a new group; as the immunisation is continued, more and more such groups are formed, more than are necessary, these latter eventually passing into the circulation. Hence, according to Ehrlich, these specific antibacterial and antitoxic bodies are merely a collection in the blood of such atom groups of the cell protoplasm as have a maximal specific affinity for the toxine. This explains why the process of immunisation must be continued to obtain an immunising blood, and why the immunising power of the blood ceases before the immunity, and also why it is that in hydrophobia the cord retains its immunising power longer than does the blood. The delicate chemical relations and affinities involved become evident, if it be remembered that no crystallised poison, no poisonous alkaloid, glucoside, or other well-defined substance is capable of producing antitoxines. Enzymes and toxines alone can do this. These substances can only act as poisons if they find in certain cells atom groups capable of binding certain noxious atom groups of these substances; this explains the long incubation period characteristic of some intoxications with these substances: it takes some time before the toxic atomic group becomes anchored.

(c) *Specific passive immunity.*—Why or how is the serum of a highly immunised animal capable of conferring upon another animal of the same or a different species an immunity against the bacterium or its products, which were used for the immunisation of the animal supplying the serum? It may be recalled—(1) that the serum obtained from an animal immunised by increasing doses of toxine is both a strongly antitoxic and an almost equally strongly antibacterial

immunising agent, but (2) that the serum obtained from an animal immunised by increasing doses of bacteria is a highly antibacterial but much less antitoxic agent, its antitoxic power varying mainly with the toxogenetic properties of the bacteria used; and (3) that the serum of the immunised animal, like that of any normal animal, is capable of producing a temporary, more or less local and slight non-specific antitoxic and antibacterial immunity.

The process of immunisation, whether toxines or bacteria be used, is a chemical one, but the chemical substances not being identical, the changes produced in the serum differ. In the one case (toxine immunisation) a solution which contains (a) large quantities of the excreted or secreted poisons, and (b) also large quantities of bacterial cell substances, is used; while, in the other case, a solution which contains (a) mainly bacterial bodies, and (b) no more toxine than happens to be in the bacterial cells. Naturally the injected bacteria will produce a little more toxine, and the effect of this must be added. The serum of an animal immunised with bacteria, therefore, possesses substances capable of counteracting in the body the intracellular poisons, and deprives the bacteria of one of their formidable weapons; and if their other weapon, the intracellular poison, is blunted, or is too weak or insignificant in amount, the animal survives, because its tissues by an inflammatory reaction can cope with the harmless foreign bodies; but if this latter weapon is powerful enough, the animal not being protected against it will surely die. Hence it follows that to give a useful immunising serum, an animal must be immunised with the extracellular poisons which contain both toxine and bacterial substances; then the tissues are guarded against both weapons.

Reactions of immunising serum.—Taking the pre-eminently antitoxic serum first, it has been shown that it is capable of rendering a poison harmless, either when mixed with it in the test-tube or when injected before or after it; a certain amount of serum will neutralise a certain dose of toxine with almost mathematical accuracy, and no more; if the serum be injected first and the poison later, smaller doses suffice than if the two are injected simultaneously; and, again, if the two are injected in the same situation, smaller quantities of serum are required than if they are injected in different situations; the serum is fairly resistant to heat and putrefaction; boiling, however, destroys the antitoxic power. If proper quantities of antitoxin and a toxine resistant to boiling heat (snake venom) be mixed, and subjected to a temperature of 100° C., the antitoxine is destroyed, but the toxine remains intact. Then, too, it requires different quantities of antitoxine for animals of different susceptibility to counteract in the body the same amount of toxine; it is evident, therefore, that the power of antitoxine does not depend on a chemical union which might be effected in the test-tube by adding one to the other, but on something else.

The pre-eminently antibacterial serum is effective when serum and culture are mixed together, or one is injected before the other, but that the quantity of serum, just as explained for the antitoxic serum, varies according to the method and site of inoculation used; heating for twenty hours at 60° C. does no material damage to the activity of the serum in the animal body, although boiling destroys it at once; putrefaction and weak antiseptics ($\frac{1}{2}$ per cent. carbolic) have little effect.

A serum possessing marked bactericidal powers shows certain interesting reactions with bacterial cultures in the test-tube or on the microscopic slide. Thus the addition of a serum obtained from an animal immunised with cholera cultures to a suspension of cholera vibrios (1) renders them motionless, (2) causes them to collect in thick clumps or clusters, and (3) finally converts them into granular bodies or masses. The serum exerts a paralysing or agglutinating action upon the vibrios. The same phenomenon has been demonstrated for numerous (mostly motile) organisms and their respective specific immunising sera. It must be mentioned, however, that normal serum may display the same power, but only when used in high degrees of concentration,

while of a highly active immunising serum only, almost immeasurably small quantities may be necessary. The processes underlying these curious phenomena are as yet not satisfactorily explained, and it must suffice to state that the agglutinating action and the immunising do not necessarily go hand in hand; indeed, on heating the serum to 60° C., which destroys the agglutinating action, the immunising power is not interfered with.

Further, such a serum often exhibits considerable bactericidal powers in the test-tube, which, like the less considerable bactericidal power of normal serum, is destroyed by heating it to 60° C., a temperature which does not materially interfere with the immunising power. Hence the latter cannot depend merely on this direct antiseptic activity. This is further proved by the fact that the normal serum of many animals possesses strongly bactericidal powers upon organisms which are often very virulent to such animals, and yet devoid of all but the most primitive immunising power. Again, dilutions of immunising serum with broth, which have lost bactericidal power in the test-tube, are still highly active in the animal body. Hence there can be no doubt that the immunising effect is to be explained by something essentially different from the agglutinating and bactericidal action.

It follows that the effect of the antitoxine and antibacterial substances depend on reactions which occur in the body; outside the body the antagonistic substances are inactive, because they do not meet the necessary chemical conditions to bring them into play.

1. When a serum obtained from an animal immunised with certain bacteria is mixed with the same cultures, Pfeiffer showed that the organisms, if motile, become paralysed and agglutinated, granular, and eventually disappear altogether, even after the serum has been heated and its natural bactericidal power destroyed. This takes place often with astounding rapidity, in the early stages of the process, without the intervention of the phagocytic cells. It must be assumed that the tissues cause the splitting off from the serum of the substances necessary to bring about directly or indirectly the destruction of the bacteria. Probably this process is an indirect one, in the sense that the substances split off combine with the toxic bacterial substances, forming atoxic compounds, the bacteria themselves thus becoming for the time being harmless and a prey to the normal defensive mechanisms, which too are considerably increased by the accompanying inflammatory reaction. If the tissues fail to produce this splitting off, paralysed by an excessive dose suddenly administered, or by the strong toxines contained in the dose, or by previous interference, the bacteria proliferate, produce their toxines, and destroy the animal. As Pfeiffer puts it, the immunising substances are present in the specific serum as an inactive modification; but, under the necessary chemical stimulus, this is converted into an active form; these substances, indeed, may be compared to inactive zymogen granules, which, upon the necessary excitation, become converted into an enzyme, and the latter meeting with chemical substances of certain similar stereo-chemical substances, elaborates fresh compounds, chemically and physiologically different from both the enzyme and the medium upon which it acts. Similarly, the inactive modification of the immunising substance becomes converted upon the adequate tissue stimulation into the active modification, and this meeting in the bacterial substances an atom group of similar configuration, binds them and forms new atoxic bodies. This action having taken place, the bacteria, as explained, are destroyed by ordinary defensive mechanisms, or perhaps also as the yeast cell by the products of fermentation. Here, as in fermentation, the concentration of the fluid is of importance.

2. The action of the antitoxic serum in the body may be explained in the same manner, and this is the explanation to which Ehrlich inclines after a prolonged study of the antitoxines. It is not known how the tissues liberate the active antitoxic substances, but once free, their effect appears to depend on their power of combining with the poison molecule. There must be atom groups of

certain configuration in the toxine, possessing a maximal affinity for similar atom groups in the antitoxine, the two fitting one another, in Fischer's words, like lock and key. It has been seen that the specificity of immunising serum is not absolute. Thus the robin antitoxine acts as powerfully against robin as ricin antitoxine. This apparently exceptional fact may be understood, if it be assumed that although robin and ricin are different substances, nevertheless the configuration of some of their atom groups is so similar, or even identical, that they must produce during immunisation an antitoxine capable of action upon either substance. The production of immunising substances, therefore, shows many analogies to fermentation; the toxines resemble enzymes to begin with, and the action of these substances presents equally strong resemblances to fermentation.

Inherited immunity.—There is no doubt that an active immunity, whether from infection or intoxication, specifically acquired, is transmitted to offspring. If the immunisation of the mother be begun after impregnation, and continued during gestation, the offspring will be immune; and, further, the immunity, so far as unequivocal experiments show, is only transmitted through the mother by the blood, and not through the father; it is correlated to the maternal immunity and varies directly with it, whatever the condition of the father; and, as proved by Ehrlich and others, it is almost always passive; the immunising substances in the maternal blood are, so to speak, pumped or passed into the fœtal tissue; the toxine itself seldom passes the placenta, only the immunising substances. Like every passive immunity, the inherited protection is transient, and the young soon lose it after they cease from suckling. Immunising substances have also been found in the eggs of hens inoculated against diphtheria or chicken cholera, which is not surprising, because, after immunisation, protective substances are found in the blood and in many tissues. Therefore, in the case of birds also, it is evidently as a rule a transmitted passive immunity. An active immunisation of the fœtus is of course possible, but it is rare and probably occurs only with bacterial immunisation. It may be assumed that in special cases bacteria pass through the placenta barrier and into the fœtus, whose tissues eventually triumph, leaving an active immunity behind. This is evidently not an inheritance of an acquired character, but merely a process of intra-uterine immunisation.

This may afford an explanation of Colles' law, namely, that the non-infected mother of a syphilitic child becomes immune: this is passive immunisation of the mother through the fœtus. "With the sperma, and not in the sperma, the syphilitic virus is transmitted to the ovum or embryo, the latter becomes infected and immunises the mother," because an antitoxine is formed in the fœtus and is taken up by the maternal blood.

There is a further factor which must not be lost sight of, namely, that since the milk of immunised mothers contains immunising substances, and since, as has been experimentally shown, those, at least for certain infections and intoxications, can produce a passive specific immunity when administered per os, the milk is the main vehicle which conveys the passive immunity to the suckling child from the mother. The child is born possessing a passive immunity, handed over to it *in utero* from the maternal blood; after birth this passive immunity is kept up and even raised through continued suckling. This accumulated suckling immunity is of somewhat longer duration than the ordinary intra-uterine immunity, because the quantity of protective substances consumed with the milk is considerably greater. In studying inherited immunity, two important factors have to be kept in view—(*a*) the placental, and (*b*) the mammary passive immunisation. With regard to inherited toxine immunisation, these points must be regarded as practically settled by Ehrlich's careful researches; for the hereditary transmission of bacterial immunisation they probably apply with equal force; the experimental proof, however, is as yet incomplete. There is certainly no evidence that the immunity acquired *in utero* is an inheritance of an acquired character.

SERUM THERAPEUTICS.

It was early pointed out that the serum of artificially and actively immunised animals is effective, even when used after the process of infection or intoxication has already begun, and then that the curative power of such serum is considerable, and that if the treatment be not begun too late, or the amount of toxine or bacteria be not excessive, the animal may be saved.

Action of curative serum.—It has been seen that active toxine immunisation produces a serum possessing both antitoxic and antibacterial properties, while an active bacterial immunisation produces a serum possessing mainly antibacterial and only slightly antitoxic properties. If, therefore, the object be to cure a bacterial disease where intoxication plays the chief part, *e.g.* diphtheria and tetanus, a serum possessing strongly antitoxic power must be used. If, on the other hand, the disease is produced by bacteria which in the animal body display a comparatively feeble toxic action, *e.g.* streptococcal and pneumococcal infections, a serum possessing antibacterial powers must be utilised. As yet there are no means existing of obtaining the active extracellular poisons of certain pathogenetic bacteria, such as the typhoid bacillus or the vibrio of cholera, and it has been impossible to find sera possessing more than an antibacterial action. With such sera, infections with several times the lethal dose of the bacterial cultures may be cured, but at present the fight against the toxines, elaborated by these organisms, has practically been a failure.

Diphtheria and tetanus are essentially intoxicative lesions. In cholera and typhoid fever the toxæmia is also marked, so that in these diseases an antitoxic serum, which moreover also always contains highly antibacterial substances, is required. On the other hand, pyogenetic lesions are less distinguished by their toxic effects; hence an antibacterial serum may prove efficacious.

Experiments on animals with the poisons of tetanus, diphtheria, ricin, etc., have shown that there is a *quantitative* relation between the toxine and the antitoxine; for each species of animal a certain dose of toxine is neutralised *in vitro* by a certain dose of toxine and antitoxine, and no less. This mixture, injected into the animal, does no harm. If, however, after the injection of toxine, the antitoxine treatment is commenced, only when symptoms of toxæmia have appeared, it is found—(1) that much larger doses than those previously calculated are required; and (2) that, after a certain period has elapsed, no amount of antitoxine will save the animal.

It must be clearly understood that the curative effect of antitoxine is much more difficult to obtain than the protective action, and that, therefore, when disease has begun, much more energetic treatment is necessary. The *curative* action of the serum depends upon the fact that the antitoxic substances are able *to tear away* the toxine molecules from the protoplasmic atom groups to which they have already become anchored. The immunising effect depends upon supplying the body with so much antitoxic substance as is (with its greater affinity for toxine) necessary *to bind* the toxine molecules, so as to prevent them from finding their affinities in the tissues of the body. It is clear that when the toxine has already entered into loose combination in the body, it must require a large excess of antitoxine, first to tear it away, and then to bind it firmly. If the combination between

the toxine and the tissues becomes firmer, more and more antitoxine is required, and a time must come when the toxine is so firmly anchored that it can no longer be dislodged, and the antitoxine attracts it in vain.   Dönitz demonstrated that the tetanus poison is fixed by the tissues from the moment it enters the blood, and that, after a copious administration of poison, a lethal dose has entered into combination in from four to eight minutes.   The latter may, however, still be drawn away from the tissues by using ten to four hundred times as much antitoxine as is required for neutralisation in the test-tube.   The antitoxic serum is therefore a true remedy, because it can remove the toxine even when it has already entered into fatal combination.   Antitoxine, then, is not merely an immunising agent, and when it is used as a curative drug its effect does not depend merely on the result of a race between intoxication and immunity.   Here the problem is probably a chemical one, analogous in many respects to fermentation.

Antitoxine does not directly destroy toxine in the test-tube.   There is no question of direct action.   If a mixture be made of pyocyaneus toxine and pyo-cyaneus antitoxine, or of snake poison and antivenin, in such proportion that the mixture is perfectly harmless, heating destroys the antitoxine, but not the toxine. It is in the living body, then, that the toxine and antitoxine are brought together; and, according to Ehrlich, antitoxine is an antidote which, physiologically and chemically, is an indifferent substance, which neither destroys nor precipitates the poison, and yet is capable of rendering large quantities of poison harmless to the living organism.   Roux and Büchner believe that, since in mixtures of toxine and antitoxine, which are physiologically neutral, both components are present unaltered, the antitoxine has an indirect action, stimulating and altering the cells, they say, so as to render them immune against the toxine.   This view is, however, hardly tenable.   Ricin causes defibrinated blood to coagulate, and cobra poison prevents blood from coagulating; but antiricin and antivenomous serum neutral-ise respectively the action of these toxines in the-test tube, if quantities are used which also exactly neutralise each other in the animal body.   Coagulation, as studied in the test-tube, is. not a vital phenomenon; hence these experiments show that the action of the antitoxines cannot depend on cellular immunisation, but that toxine and antitoxine react upon each other directly and chemically. Further, Ehrlich has shown that this union of toxine and antitoxine in the test-tube is quicker in concentrated than in dilute solutions, is accelerated by warmth and delayed by cold, the union becoming firmer the more concentrated the toxine and antitoxine, and the longer they have reacted upon each other.   Analogous examples occur in pure chemistry, especially in the formation of double salts.

Specificity of antitoxine.—If toxines · are specifically different, their antitoxines are also specific in their action.   Hence a diphtheria antitoxine is of no avail in tetanus or snake poisoning.   The specificity of antitoxine is based on a firm experimental foundation.   Yet it is found that an anticobra serum will ,act against all snake venoms, and even against scorpion poison, and that antirobin serum will act against ricin as well as against robin.   An explanation of this is that—(*a*) all snake venoms are closely allied to one another, daboia poison forming perhaps the cnly excep-tion; and (*b*) scorpion poison and robin may, chemically, be derivatives of cobra toxine and ricin respectively, each corresponding in its structure to a body produced by' a shifting of the atom complex of snake poison or ricin, *i.e.*, to use Ehrlich's nomenclature, they may be toxoids of their respective toxines.   It is easy enough to manufacture toxoids from toxines, which may be quite harmless, and yet are capable of producing an antitoxine, and

also of binding the antitoxic substances; and it is therefore quite possible that many toxines in nature represent the toxoids of other stronger toxines. This would readily explain the vicarious immunity which exists between intoxications.

The precision with which the antitoxine picks out the cells injured by the toxine, which their affinity for the latter has attracted, is little short of marvellous. In the motor cells of the cord, for instance, are substances with a strong affinity for the tetanus poison. These bind the latter, thus the cells lose part of their function, especially their inhibitory control, and the toxic spasms result. Histologically, changes can be demonstrated in the cells; their granulation, which is brought out by Nissl's methylene-blue reaction, disappears or fades. If, now, at the proper moment, antitoxine be injected, the cells soon regain their granulation, and again stain normally, although their restitution is not complete until the signs of disease have quite disappeared. It is hardly possible to imagine anything more precise than this restorative action of the anti-toxine. These observations prove clearly the cellular action of toxine and antitoxine, and also that the latter is a true remedy. Antibacterial serum cannot differ in its action from that of antitoxine; the difference is merely chemical, *i.e.* the poison derived from the bacterial cell has a different chemical configuration and different affinities. It can be of use olny against these substances, and must be valueless against toxines which are altogether diverse, or do not stand to them in the relation of toxoid to toxine. By means of this serum, bacteria can be committed to sudden death. If, however, the bacteria have liberated much toxine, the animal will die, since this serum does not protect against the toxine. Therefore, in practice, an antibacterial serum is of no avail in diseases where toxæmia evidently exists. Thus in man enteric fever is essentially a toxæmia; hence it is but little or not at all affected by the anti-typhoid serum derived from a horse immunised with cultures of the typhoid bacillus. Success must therefore not be expected, or hope held out from methods which science points out are based on errors of judgment.

Serum treatment.—Of serums for diphtheria, tetanus, plague, typhoid, cholera, streptococcus infections, pneumonia, snake poison, tuber-culosis, and syphilis, not to mention rabies, the only ones that have a right to figure as of remedial value are the diphtheria, tetanus and anti-venomous sera, which are all antitoxines. Clinically, the diphtheria antitoxine has achieved so much that its usefulness can no longer be doubted, except by the most prejudiced and blinded physician. Tetanus antitoxine, used clinically, has so far been accompanied by but limited success, and has failed in severe cases, and the anti-typhoid and cholera sera have been condemned as useless, for the reason stated above. Anti-streptococcus serum has of late been extensively used, but at present it is impossible to speak of its value in decided terms. Some observers claim that it has done good, others condemn it; it is certainly only an anti-bacterial serum, and therefore cannot do much good when the toxæmia is acute; and again, the physician must always convince himself that he is dealing with a streptococcus lesion, and, while using the serum, must make the necessary bacteriological investigation. Similarly, it is too early to speak of the anti-pneumococcus serum, or of that supposed to act against plague and tuberculosis. Yersin declares that his serum has been of considerable use in plague, while others deny or doubt this. The attempts to prepare an antisyphilitic serum are interesting, but have as yet not

passed beyond the experimental stage. Antivenomous serum, it is said, has already been successfully used in more than one case of snake bite.

When using curative serum, the physician or surgeon should clearly understand the dosage. The serum, if properly and carefully prepared, is absolutely harmless to the normal individual. More will be said of its possible dangers and complicating effects later. While dealing with an otherwise normal patient, even large quantities can be injected, so long as this is done aseptically. The amount to be administered must not be measured by drachms, ounces, or cubic centimetres, but by immunising units. The physician must therefore understand the meaning of this unit. The standard employed for antitoxic serum is that elaborated by Ehrlich, and, according to this standard, an immunising unit is that quantity of serum which is capable of neutralising one hundred times the minimal lethal dose of the original standard toxine for a half-grown guinea-pig. It is essential that no serum be used unless its antitoxic value has been carefully estimated; and experiments show that for clinical use concentrated sera are preferable, that is, sera which contain a large number of units in a small bulk. Such sera can only be obtained from animals which are not only strongly immunised, but also before the immunisation possessed a marked susceptibility. The number of units to be used in each case varies with the severity of the symptoms, and it is impossible to give hard and fast rules. At the present time three forms of serum are clinically employed in this country, namely, diphtheria antitoxine, tetanus antitoxine, and antistreptococcus serum; and a few general remarks as to dosage may fitly be made here.

1. **Diphtheria antitoxine.**—1500 to 2000, or even 4000, units should be the *minimum* dose, and this should be given early, and, if necessary, frequently repeated until all danger is past. The number of units that may be given must of course depend on the supply of serum.

2. **Tetanus antitoxine.**—Here it is absolutely necessary to use an extremely powerful serum, and a very large dose, as measured by units, must be administered immediately. Intravenous or intracerebral injection holds out more hope of success; in all but very slight cases the latter method of administration is therefore especially to be commended. Further injections may be given every twelve hours. The intracerebral treatment should be resorted to, unless the first injection is made within thirty-six hours after the onset of the spasms.

3. **Antistreptococcus serum.**—This being an antibacterial serum, large doses should be used. As yet, there is no good standard for these antibacterial sera; therefore a serum which is known to be active in extreme dilutions, when tried on laboratory animals, should be obtained, and of this, so far as our present knowledge goes, however strong the serum proves to be, 20 c.c. should be injected subcutaneously every twelve hours, until improvement sets in.

In every case where a serum is used, the ordinary rules of treatment must not be lost sight of; the serum is an adjunct, but not a charm. No local antiseptic measure must be omitted; no operative measure, such as tracheotomy, amputation, or incisions, must be postponed; no generally approved medicinal treatment neglected. There has been a tendency to regard the antitoxic or other sera as omnipotent, but it must be remembered that they act best in the normal body, and when the poison to be neutralised is not present in excessive amount. General and local treatment tend to bring the body nearer its normal state, and to reduce the elaboration of more poison. The antitoxine is anything but the fool's weapon! That, in making injection, strict aseptic and antiseptic precautions must be observed, goes without saying. The skin must be thoroughly washed, and the syringe, serum, and everything else used must be absolutely sterile.

Results.—A few examples of the results of serum treatment may be given.

Diphtheria.—The prognosis in cases of diphtheria treated with anti-toxine is far better than at any time previous to its introduction as a method of treatment, especially in dangerous forms of the disease (namely, those under five years of age, and those in which tracheotomy is required), and in the case of those in whom treatment is begun early in the disease, and when sufficiently large quantities are injected. The proper administration of antitoxine reduces the mortality considerably, and assists the older methods of treatment. The fact that Liebreich and others object that the new treatment has not fulfilled its original extensive promise, should not carry much weight. That it has reduced the mortality considerably, speaks for itself. Every case cannot be cured, for when vital damage has been done the antitoxine cannot manufacture new tissues, nor can the diphtheria serum cir-cumvent or cure the secondary infections which only too often destroy life. Streptococcus septicæmia is a common cause of death in diphtheria. Unques-tionably there is no better form of treatment in diphtheria than to combine the administration of antitoxine with the older methods. Welch expresses himself thus: " The study of the results of the treatment of over 7000 cases of diphtheria by antitoxine demonstrates beyond all reasonable doubt that antidiphtheritic serum is a specific curative agent for diphtheria, surpassing in its efficacy all other known methods of treatment for this disease. It is the duty of the physician to use it ! It should be forcibly brought home to those whose philozoic sentiments outweigh sentiments of true philanthropy, that those discoveries which have led to the saving of untold thousands of human lives have been gained by the sacrifice of lives of thousands of animals, and by no possibility could have been made without experiments upon animals."

Tetanus.—The serum treatment has not materially or actually changed the prognosis in acute and serious cases; but in milder cases it lessens the spasms, the pain and distress, and, it seems, reduces the mortality, but to what extent cannot be · estimated until statistics of a larger number of cases have been collected. Furthermore, the antitoxine may pull up a case which is rushing away into acuteness, and increase the chances of older forms of treatment, such as amputation, morphine, and chloral. It should certainly be used in all but hopeless cases. Up to March 1895, the mortality of acute cases of tetanus, in spite of the antitoxine treatment, amounted to 85·7 per cent.; but in chronic cases it had been reduced to 5·7 per cent., so that with the antitoxine in milder cases better results are obtained than with methods of treatment which omit the new remedy; and since, to use Roux's words, " dans la pratique on ne choisit ni le cas ni le moment de l'intervention," it is clearly a duty to combine the serum treatment with other recognised therapeutic methods.

Streptococcus lesions.—The numbers of cases reported are too small, and the opinions expressed too contradictory, to allow of a definite state-ment that the antistreptococcus serum is a remedy which it is the physician's or surgeon's duty to use. It is difficult to judge statistically of the clinical effect of antistreptococcus serum, because in many cases a bacteriological examination has been regarded as superfluous. Some observers go so far as to maintain that even during natural recovery from streptococcus infection, the serum acquires no protective substances. Koch and Petruschky inoculated a patient first with a large dose of anti-streptococcus serum, and twenty-four hours later with streptococcus

material, and repeated this with various sera; in no case did the serum afford the slightest preventive action. There are, however, a number of cases recorded where prompt fall of temperature and recovery have followed so quickly upon injections of the serum, that it is very difficult to disbelieve altogether in its efficacy. According to Mr. E. A. Steele, of twenty-six cases of puerperal septicæmia, unfortunately not bacteriologically examined, only ten died; recovery from infective endocarditis has also been recorded. Since the serum is practically harmless, it may be used in dangerous cases of streptococcus infection as an additional aid, though the outlook in this direction is not very hopeful, since this serum contains no antitoxic substances.

It is to a certain extent unimportant where the serum is injected. Generally it is administered subcutaneously, and in that case the buttock may be chosen or the abdomen, parts on which the patient does not rest, and in which the muscles may be kept quiet. In some serious cases it may be advisable to practise intravenous injection, but this has as yet not found general approval, although when the toxæmia is severe it would probably be more efficacious than a subcutaneous administration. Some observers claim that in animals the antitoxine may exert its action even when given by the mouth. This is, however, an uncertain method of administration, and the experimental evidence is by no means strong enough to justify its recommendation; furthermore, it would require very large doses to be of any value, and at best this method of treatment would be costly as well as doubtful.

The serum may be used liquid or dry. In the latter case it must be dissolved in a small bulk of sterile water (2–5 c.c.), and strict cleanliness and antiseptic precautions must be observed; the water should never register higher than the body temperature, as heating destroys the action of the antitoxine. The serum is not very sensitive to light and the ordinary changes of temperature, and may be kept for some time, though it usually loses in power, especially for the first year. A turbid liquid serum should never be employed, because this generally means bacterial contamination. The dry serum, which is very stable when dissolved, is always turbid, and must not be filtered, but used immediately the solution has been made. A bottle of serum should only be used once, *i.e.* it should not be opened and then put away for further use. As a matter of fact, each bottle never contains more than a single dose. When the injection has been made, the parts should not be kneaded, under the impression that this will hasten absorption. If intravenous injection has been decided upon, a liquid serum should be used and not a dry one, for fear of embolisms. A syringe should be chosen which will contain the entire dose, necessitating only a single puncture; the piston must fit tightly, and on no account should air be injected. These are a few general rules, which the physician must observe unhesitatingly.

Complications.—Among the alleged ill effects which have been attributed to the use of serum, the most important are the following:—Rashes, joint affections, inflammation about the seat of inoculation, abscesses, albuminuria and nephritis, collapse and sudden death, and pyrexia. First it must be said that with the improvements in the methods of obtaining and preparing the antitoxine, these complications are steadily decreasing, although the number of patients treated and the amount of antitoxine has considerably increased. Experiments and experience have shown that antitoxic serum, as far as toxic and constitutional

symptoms are concerned, act exactly like ordinary normal animal serum. The rashes which undoubtedly appear are not due to the antitoxine contained in the serum, but are due probably to substances in normal horse serum. These substances can be partially avoided by using highly concentrated serum, *i.e.* one containing a large number of units in a small bulk.

Joint affections are now extremely rare, inflammation and abscesses are avoidable, and are not due to the antitoxine; albuminuria and nephritis appear to be symptoms of the disease rather than effects of the antitoxine. Collapse and sudden deaths have occurred, but these must be due to some idiosyncrasy on the part of the patient, and can count for about as much as the rare deaths that ensue from the use of ether or chloroform. The essential harmlessness of the serum has been sufficiently demonstrated by hundreds of thousands of injections; and what little harm there is in serum will no doubt in course of time be remedied altogether, when pure antitoxine or serum is obtained of such concentration that minute doses are sufficient to contain the required number of units.

TOXÆMIA.

The symptoms and lesions of infective diseases are due mainly to the toxines manufactured by the bacteria, and not to the mechanical presence of these bacteria. The diseases associated with infective micro-organisms are produced by processes of intoxication. Many other lesions and diseases, or their symptoms, are, however, caused by poisons, to which it is necessary to devote a few words.

Nature of poisons.—Poisons may either be introduced into the body, as such, from without, or they may be manufactured in and by the tissues themselves, whence they are absorbed. In the latter case they may be formed either during the ordinary metabolic activity of the tissues, or during normal fermentative processes set up by the tissue enzymes, or by bacteria which must be regarded as normal inhabitants of the digestive tract; or, again, they may be the products of an abnormal metabolism or abnormal bacterial fermentation, or of pathogenetic bacterial activity. These poisons may be classed as follows—

I. **Exogenous poisons,** *e.g.* arsenic, alkaloids, snake poisons, etc.
II. **Endogenous poisons**—
    (1) Metabolic—(*a*) Normal metabolism = waste products.
               (*b*) Abnormal metabolism = cachexia strumipriva, uræmia, cholæmia, diabetic coma, etc.
    (2) Tissue fermentation = enzymes, albumoses, etc.
    (3) Bacterial fermentation—(*a*) Normal = products of bacterial action in digestive tract.
               (*b*) Abnormal = intestinal fermentations.
    (4) Pathogenetic bacterial activity = infective diseases.

The action of a poison appears undoubtedly to depend upon chemical affinities existing between it and the tissues, or some elements of the tissues. Irritants or agents which act directly by causing immediate death of the tissues with which they come in contact, must not be included amongst the poisons, but only those substances which, whatever their local action may be, have a distant or remote action upon the blood or internal organs. This remote action may show itself (*a*) in organs whose function it is to retain or excrete the poison, or (*b*) in organs which are not possessed of such function, and therefore must be supposed to have

a special affinity for certain poison molecules. This explains the remarkable selective action of certain poisons—lead, strychnine, tetanus toxine, diphtheria toxine, and snake poison (all show great affinity for the nervous system), phosphorus, arsenic, and antimony for the blood, liver, kidneys, and heart. Again, of the nerve poisons, some select the peripheral, others the central system.

We may therefore distinguish between poisons which act primarily—(1) on the blood; (2) on the heart; (3) on the nervous system—(a) on the peripheral nerves (motor or sensory), (b) on the spinal cord, (c) on the medulla, and (d) on the brain itself; and (4) on the protoplasm generally. These last are general poisons, and may act chemically—(1) by oxidation (phosphorus and arsenic); (2) by catalysis (chloral, ether); (3) by formation of salts (salts of heavy metals); or (4) by substitution (hydrocyanic acid, phenoldiamine). There are also the special poisons which select only certain elements and molecules, and do not act on the protoplasm generally.

In the case of tetanus, it is evident that in the motor cells of the spinal cord there must be atom groups which possess a specific affinity for the tetano-toxine, while the other organs of the body show no such predilection. The special poisons differ as greatly in their chemical constitution as in their action. Some are crystalline poisons, alkaloids, glucosides, and such well-defined chemical substances, which cannot produce antitoxines; others are the toxines, ferments, and toxalbumins, all of which have the power of producing antitoxines.

The general effects of an intoxication in bacterial infections may now be considered. The products of bacterial activity include not only the specific toxines, but also other poisonous substances, and at present it is impossible to separate the two groups. There is a tendency on the part of those studying a disease to fix the attention on the obvious effects, and to neglect the secondary or remote and general effects ; and yet, as regards treatment and convalescence, a thorough understanding of the effects of a bacterial toxæmia is absolutely necessary. In typhoid fever, for instance, besides the typical temperature curve, the intestinal symptoms, the prostration, collapse, and mental changes, the toxines of the typhoid bacillus and its associates in the bowel produce anatomical changes beyond those found in the gut. There are changes in the liver, kidneys, muscles, and perhaps also in other tissues, all of importance ; and it may require long and careful treatment during convalescence to restore the organs to their normal condition. The delayed recovery from a fever undoubtedly depends on the intensity of the general toxic effects, and a patient is not cured until these have entirely disappeared. Many bacterial poisons, in doses not sufficient to cause death, produce marasmus, not due to the specific but to the general action of the poison, this condition always occurring in all but the slightest intoxications. The immediate dangers of an infection may have been averted, but the patient has still to be carefully watched and nursed, because his organs and tissues are left in an injured and diseased condition, from which in some cases they may never recover. Many sequelæ are due to these less characteristic toxic effects ; they are often recognisable anatomically, as evidence that although the poison has been removed, its effects persist, and that during convalescence there may be very grave disease and lesions, which, if not repaired, may become progressive, and eventually declare themselves as almost certainly fatal diseases. Flexner lays stress upon these anatomical changes produced by intoxications with certain toxines, and points out that the cells of the liver and kidneys (most), suprarenal capsules and pancreas (least), are affected ; in highly differentiated cells, not all the parts of the protoplasm are equally affected by the poison. The necrosis, at least in the liver, may be followed either by regeneration

and restoration of the integrity of the organ, or, in the place of the dead cells, a new tissue develops, which leads to the formation of a scar, and in some cases a form of cirrhosis may result. In diphtheria-intoxications changes in the cardiac muscle, the liver, kidney, and suprarenal capsules, and in the nerves, may all be observed. The antitoxine may save the animal from death, but paralysis often occurs, because the degenerative changes had already gone too far: the remedy cannot build up new nerve tissues. Intestinal lesions are common, for frequently, after sublethal doses, animals, while emaciating, develop a chronic diarrhœa, which persists until the animal eventually dies. Our knowledge of the general changes produced by bacterial toxæmia is still imperfect, but so far as it goes it teaches the practical physician the important lesson that the convalescence requires as much careful attention, if not more, than the acute stages of the infective diseases.

Besides the toxæmia produced by the absorption of bacterial poisons, there are what may be called autotoxic effects, which depend upon absorption of chemical substances elaborated in and by the tissues themselves. These substances may be normal metabolic products which have been allowed to accumulate, or they may be abnormal metabolic products, or products which, under ordinary conditions, undergo further changes. During the process of metabolism there appear a number of intermediate products, such as kreatin, cystin, glycosuric acid, oxalic acid, glucose, lactic acid, etc., which normally, by oxidation or reduction, by synthesis or splitting, are converted into other bodies, but which may accumulate in a diseased organ, and thence be taken up by the circulation. During the metabolic processes of health, both harmless and noxious substances are formed, but the latter produce no ill effect, because they are either formed in small quantity, or enter into combination with other bodies, or are rapidly excreted or destroyed. If, for some reason or another, they appear in unduly large quantity, or if they are not changed into harmless compounds, or excreted and destroyed, they enter the blood stream and a toxæmia results, which is either acute and momentary, or chronic and periodical. On the other hand, poisons may arise through pathological processes, which alter the normal metabolism in such a way that new and toxic products are formed. Roughly, the following forms of spontaneous toxæmia may be distinguished:—

Spontaneous toxæmia, due to the retention of normal or physiological metabolic products (as for instance uræmia and carbonic acid poisoning).

Spontaneous toxæmia, due to an over-production of physiological or pathological metabolic substances (diabetic coma, acetonuria, cystinuria, cancerous cachexia).

Spontaneous toxæmia, due to removal or exclusion of an organ (myxœdema, acute yellow atrophy of the liver, pancreatic diabetes, Addison's disease). The thyroid gland, liver, pancreas, and suprarenal bodies are assumed to destroy toxic metabolic products, and if these glands are diseased such products must accumulate.

Spontaneous toxæmia, due to general metabolic disturbances (gout, oxaluria, diabetes).

Arranging the toxæmias according to the organ in which the poison is produced, accumulated, or through which it is retained in the body, they may be due to—

1. Cutaneous lesions—Extensive burns and varnishing ⎫ *i.e.* Retention of sub-
2. Renal disease—Uræmia, eclampsia . . . . ⎬ stances normally
3. Lung disease—Carbonic acid poisoning . . . ⎭ excreted.

4. Suprarenal disease—Morbus Addisonii . . . .   }
5. Pancreatic disease—Some forms of diabetes . .   }
6. Hepatic disease—Acute yellow atrophy, tetany, cholæmia . . . .   }
7. Thyroid disease—Myxœdema, cachexia, cretinism, Graves's disease . . . .   }

i.e. Impairment of organs which normally destroy the ordinary metabolic poisons, or secrete substances necessary for the normal metabolic activity.

8. Intestinal disease — Acute and chronic gastrointestinal lesions . . . . . . }

i.e. Abnormal fermentations and impaired absorption — putrefactive and bacterial toxines.

It may be objected that the symptoms of any disease are due to intoxication, and there can be no doubt that chemical changes accompany every organic lesion. Thus, in heart disease, when compensation breaks down and the respiratory activity is lowered, the blood is impaired, and amongst other changes there must be diminished oxidation and diminished combustion of the waste products. Such conditions are, however, not included under toxæmia, unless they are accompanied by distinct symptoms of intoxication.

It is important to know what conditions may lead to a toxæmia, on a clear understanding of which treatment must depend. Toxæmic conditions can only occur when one or more of the paths of excretion are blocked, if the activity of certain organs has been impaired or abolished, or if the amount and intensity of the poison is too great for the normal mechanism to cope with.

Under normal conditions, metabolic poisons are *excreted* by the skin (evidence derived from varnishing the skin), kidneys, and intestines; urticarial eruptions are undoubtedly due to a reaction of the skin against the excreted irritant. To some extent the lungs also eliminate poisonous substances, especially volatile gases (acetone, ammonia, sulphuretted hydrogen, the products of retrogressive changes).

Other organs *neutralise* or *destroy* poisons. The liver has the power of rendering harmless—(a) poisons which, after being introduced into the intestinal canal, find their way into the portal circulation, and (b) of modifying the toxic metabolic substances which, under normal conditions, are carried to it by the portal circulation. Speaking generally, the alkaloids lose about half their toxic power in passing through the liver, but it must be remembered that in this matter different species of animals vary considerably. It has been demonstrated that if the inferior vena cava and portal vein be so connected as to divert the portal blood into the vena cava from the hepatic filter, the animal dies of a chronic toxæmia, which in many respects resembles the uræmic condition. Here it must be assumed that the poisonous substances formed during digestion pass directly into the systemic circulation, and that an autotoxæmia results. Hence it may be concluded that, if through anatomical or physiological disturbances the filtering action of the liver is impaired or abolished, the poisonous substances of a normal or abnormal metabolism readily find their way into the general circulation.

The kidneys, besides excreting poisonous substances, possess toxine-destroying properties, transforming the toxic bodies into new atoxic compounds by processes of oxidation or reduction, synthesis or splitting. It is possible also that the kidneys are provided with a so-called internal secretion, the absence of which might lead to toxæmic symptoms.

In the intestinal tract, poisons which are not evacuated may be rendered harmless by the various secretions, such as the bile or the pancreatic and gastric juice, or they may be acted upon by the epithelium of the intestine. It has been

shown that bile and pancreatic juice have a marked action on so strong a poison as that of the cobra.

In many animals, after ablation of certain organs (thyroid, pancreas, supra-renal capsules), toxæmic symptoms appear, and it is assumed by many that such organs possess the power of neutralising poisonous substances. It may be that the phenomena which follow ablation are due to spontaneous intoxication, but this is by no means universally accepted.

The clinical picture of a spontaneous toxæmia varies considerably according to the nature and origin of the poison. The physiological action of the poisonous bodies is manifold, and furthermore the poison may be highly selective; thus it may affect more especially the heart, or the respiration, or the intestinal tract, the nervous system generally, or some specialised part, or it may be a general tissue poison. Again, the clinical picture must vary with the dose of poison absorbed and the acuteness of the absorption. Hence the protean character of certain toxæmias, such as uræmia.

Treatment of toxæmia.—(a) In the case of a bacterial toxæmia, the rational mode of procedure is to search for an antitoxine. This can only be obtained by first subjecting an animal to a slow process of intoxication, in order to bring out a specific immunity, and to impart to the serum anti-toxic or neutralising properties. (b) For some of the exogenous poisons there are true antidotes, which, when administered to a poisoned animal, form harm-less bodies with the toxic molecules, and thus save the animal from certain death. This is the ideal method of antitoxic treatment, and is well illustrated by the following example. Lang and Heymans have shown that the nitril group is highly poisonous to rabbits, the toxic phenomena no doubt being due to the hydrocyanic acid radical of the nitril. If, shortly before the expected death of the poisoned animal, hyposulphite of soda be injected, the moribund rabbit suddenly begins to improve and quickly revives. The neutralisation of the poison is due to the fact that the sulphur of the hyposulphite combines with the CN of the nitril. It must be our aim so to study the chemical nature of the endogenous poisons, as eventually to obtain substances which neutralise with the same cer-tainty as sodium hyposulphite acts upon nitril. (c) In the toxæmias which arise from inadequacy of the thyroid gland, the symptoms and effect of poisoning can be removed by supplying the material which is wanting, namely, thyroid extract. This method of treatment has been used also for diabetes, Addison's disease, and other morbid states assumed to be due to the abolition of the specific internal secretion of certain glandular organs, but so far with but little success. (d) In cases of uræmia, cholæmia, or intestinal poisoning, the only remedies at present known are those which stimulate excretion through the kidneys, intestines, skin, etc. Such methods of treatment must necessarily be uncertain, and they often fail.

Although it is possible to speak in no uncertain terms of autotoxæmia, it must be conceded that at present little is known of the poisons which are supposed to be the cause of the various forms of intoxication. Strictly speaking, the separa-tion and determination of these poisons are the necessary foundation of the doctrine of autotoxæmia, and they must be separated—(a) from the seat of lesion and from the blood, and (b) also from the urine. But in addition there must be the clinical signs or symptoms of a toxæmia. Here difficulties come in, because—(1) no poisons may be found at the seat of lesions, as they have already been absorbed or secreted, or, (2) as in their passage through the body to the kidneys, they may have been altered beyond recognition. Yet there can be but little doubt that in diabetic coma, uræmia, eclampsia, gout, and the coma of cancerous disease, acute yellow atrophy of the liver, tetany, and other con-ditions, there is an element of true toxæmia, for—(1) the clinical symptoms and pathological evidence are too convincing, and (2) the treatment of these different conditions has become more successful since the principle of intoxication was recognised. Still, autotoxæmia must not be made to include too much. Thus,

for the present, it must be left open whether the vertigo or asthma of gastric intestinal origin, or the convulsions of childhood, the lesions and symptoms of chlorosis, or pernicious anæmia, are actually due to a true toxæmia, rather than to other influences, such as nervous reflexes or general organic and functional changes. Here the guide must be the clinical symptoms, and the anatomical conditions found after death. The absence of morbid changes, together with the existence of marked typical clinical symptoms during life, must in any given case always be strong evidence of a toxæmia. Hence, however imperfect our present knowledge of autotoxæmia is in many points, it must be confessed that certain conditions can best be explained, and more successfully treated, on such an assumption. In fact, the treatment successfully adopted in such cases as uræmia, diabetic coma, or myxœdema, as above mentioned, is the strongest evidence in favour of the doctrine of autotoxæmia. Thus, where an intoxication is due to the inadequacy of an organ, its symptoms may be removed by supplying the substances withheld from the body by the diseased organ. This is done in myxœdema, which can be cured by injections of thyroid gland substance; when, however, an intoxication is due to an abnormal metabolism, the rational treatment would be either to change the abnormal products into normal ones, or to dissolve or remove the abnormal compounds. This is as yet impossible, as there are no chemical agents capable either of dissolving out the uric acid, or of permanently correcting the metabolic errors which find their expression in the uric acid diathesis. Where a toxæmia depends upon a retention or a production of toxic substances, Bouchard's maxims must be followed—(1) To inhibit the production, retention, or absorption of the poisons; (2) to destroy them by stimulating these organs whose function it is to neutralise them, or by introducing chemical substances; (3) to aim at promoting their secretion through the skin, lungs, intestines, or kidneys. How to inhibit production or absorption is at present unknown, and the destruction of the poisons already formed or absorbed can only be attempted by chemical substances, which act either indirectly upon them by stimulating the toxine-destroying organ, or directly by dissolving, precipitating, or combining with the poisonous substances so as to form atoxic bodies. Here, again, it is impossible to find substances which act upon these unknown poisons just as the hyposulphite acts upon the toxic nitril. Hence it only remains to attempt to promote a rigorous excretion of the poisons. This excretion may be furthered by diaphoresis where the skin is pervious. Nature herself gives an indication of this treatment: profuse sweating accompanies or precedes the crisis or turning point of several diseases which are pre-eminently toxic, such as pneumonia and rheumatic fever. In uræmia and eclampsia, diaphoretics and the vapour bath are recognised therapeutic measures.

Diuresis also is a good protective against the accumulation of toxic substances in the tissues. In uræmia, diuretics must be employed if the renal tissues are pervious; in diabetic toxæmia, when the urine excretion becomes diminished, they are employed, and so also in severe febrile conditions. In fact, whenever a toxæmia is accompanied by a progressive or sudden diminution of the secretion of urine or by anuria, diuretics are the rational mode of treatment. In all chronic forms of intoxication, such as migraine, uric acid poisoning, etc., copious diuresis is of the greatest help in washing out the poison or in diluting it; this is often effected by copious draughts of suitable and especially warm drinks.

A toxæmia may also be relieved by the withdrawal of blood, and this is done in uræmia and eclampsia, or in slighter forms of intoxication, such as migraine. This may be combined with infusion of saline solutions, as has been recently practised in the more acute toxæmias, such as uræmia.

Where the forms and signs of the poisonous substances are to be sought for in the intestinal tract, it is evident that an attempt should be made to limit the abnormal fermentation process or decomposition, and to remove the products of these processes. This may be done by emetics, the stomach pump, by laxatives and purgatives, or even by washing out the intestinal canal. Nature's own method

of ridding the gut of noxious substances is diarrhœa. Intestinal antiseptics have been praised by many writers, but it must be clearly understood that it is impossible to stop putrefactive processes in the human intestine by the internal administration of antiseptics. The only method of bringing about an intestinal disinfection is the removal of the foul or noxious contents, and thus it is that calomel has acquired the reputation of being the best intestinal antiseptic; it acts not by disinfection, but by virtue of its laxative properties.

But even when the source of the poison is not primarily or merely intestinal, the bowel may be used as a channel along which the toxic material may be drained away from the blood. The effect of cathartics is to stimulate a copious flow of exudation from the capillaries into the lumen of the intestine, and when kidneys and skin are both impervious, the blood itself is the last resort. Thus phlebotomy or cathartics are utilised in uræmia, and especially in eclampsia. In every case of toxæmia, the following points must be considered—(a) the cause of poisoning, and (b) the best methods of either removing or neutralising the poison. Several methods may have to be considered, and due attention must be paid to the diseased organ or organs; in fact, it is of primary importance to investigate the organic lesions before making a hypothetical diagnosis of toxæmia, for the latter must never be made without having a clear understanding as to where and how it has arisen.

Treatment by means of Organic Extracts.

In the previous section it has been mentioned that some forms of disease are due to morbid changes in, or the complete removal or exclusion of, certain glandular organs, such as the thyroid; and it is generally assumed that in such cases the disease is of the nature of a toxæmia. What is the evidence, clinical and experimental, which proves that the existence of such glandular organs is necessary to the continuance of life?

Thyroid gland. —Experiments on animals, suggested through observations on man, have conclusively shown that total extirpation of the thyroid gland, together with the accessory glands or parathyroids, is a fatal operation. The symptoms following the removal may be acute or chronic. In monkeys, as shown by Horsley, when the changes are acute, tremor, paroxysmal clonic spasms, paralysis, paræsthesia, sluggish mental operations, passing on to apathy, lethargy, and coma, subnormal temperature, and visible trophic changes ensue. When the changes are chronic, the monkeys resemble cretins, and become dull of intellect, although at times they have periods of idiotic activity. The symptoms vary in different animals; but it suffices to state that total ablation of the thyroid tissue is invariably followed by characteristic symptoms, and in most cases by death. Partial extirpation, on the other hand, does not lead to disease or death, if an adequate amount of thyroid tissue is left, so that, as will be discussed more fully under myxœdema, the thyroid gland is a vital organ without which life is impossible. By previous successful implantations of thyroid tissue in the abdominal cavity, the effects of total removal may be prevented.

The changes produced in animals have been explained as being due to intoxication or toxæmia, for it has been shown that the urine of animals deprived of thyroid tissue is more toxic than that of normal animals, and that the blood of animals which suffer from tetany after thyroid ablation, transfused into normal animals produces tetany in them.

Experiments have also shown that intravenous and subcutaneous injections of an extract of normal thyroid tissue may remove the consequences of a thyroidec-

tomy, or, at any rate, keep them in abeyance, so that there can be no doubt that this extract possesses a curative action, *i.e.* that the toxic symptoms following upon ablation of the thyroid gland may be neutralised by supplying those chemical substances of which the removal of the gland has deprived the tissues of the animal.

The observations which have been made on animals are in close agreement with those made on man. Clinical observations, medical and surgical, showed that atrophy, inadequacy, or extirpation of the thyroid gland results in myxœdema or a cretinoid state, tetany, or cachexia; subsequently animal experiments proved conclusively the vital importance of this gland. Further observation and experience showed that the lesions and symptoms due to inadequacy of the thyroid gland may be allayed or removed by implantation of thyroid tissue, by injection of an extract of the gland, or even by gastric administration of the active principles. Hence it was concluded that the thyroid gland secretes a substance which is necessary for the proper metabolic activity of the body, and that if this substance is not secreted in sufficient quantity, it must be artificially supplied by inoculation or feeding. Since the thyroid gland has no excretory ducts, its secretion must be directly absorbed by the lymphatics; the product of its activity is an internal secretion.

If this internal secretion is absent or insufficient, there results myxœdema, or cretinism, tetany, or the cachexia thyreopriva. How this secretion works is at present unknown. At first in the treatment of the lesions produced by thyroid inadequacy the whole thyroid gland was used, but gradually attempts were made to obtain the active principle. The thyroid gland forms a chemical substance, probably an iodine compound, which is absorbed and is essential to life, and when this substance is absent or insufficient it must be artificially supplied. Inadequacy of the thyroid secretion leads to metabolic disturbances, which may be acute or chronic. When acute, the picture is one which may well be compared to an intoxication or toxæmia; and when chronic, to a cachexia, which after all is a form of intoxication. When the thyroid secretion is withheld, there follow trophic degenerative changes in various tissues and organs, the skin, and subcutaneous tissue, the reproductive organs, etc.; further, that the administration of thyroid substance completely alters the metabolic chemistry of normal or diseased man or animal, is now undoubted, as may be seen from the effects of the thyroid treatment in many cases of obesity, in which it may cause a considerable diminution of the fat stored up in the tissues, and from the effects which occasionally accompany the administration of thyroid substance to normal individuals. In myxœdema the treatment causes a marked increase in the nitrogen elimination, and removes the marked trophic retrogressive changes as well as the toxic symptoms.

Whatever the final explanations may be, these observations and facts afford a new principle of treatment; they have shown that it is possible by inoculation or feeding to artificially replace a substance which is necessary for life, and which is directly secreted into the tissues. Further, in the case under discussion, the substance used for treatment may be supplied by animals belonging to altogether different species, although there are distinctions based undoubtedly upon the comparative chemistry of the thyroid gland. Finally, it is obvious that the artificial substance must be administered as long as the normal supply is inadequate, *i.e.* at repeated intervals and for a long period.

Pancreas.—Observations and experiments of recent years have shown that the pancreas is a vital organ. Complete extirpation of the pancreas causes death of the animal after a short illness, accompanied by all the typical symptoms of diabetes; partial ablation, however (leaving an adequate amount of pancreatic tissue behind), is not fatal, and produces no diabetes. It has also been conclusively proved that the symptoms which ensue are not due to the absence of the ordinary pancreatic secretion which, under normal conditions, finds its way into the duodenum, for ligature or complete experimental obstruction of the pancreatic duct does not cause diabetes. Nor is the experimental diabetes due to nerve lesion, for section of all the nerves around the pancreas does not produce it. Hence pancreatic diabetes must depend upon the elimination of a special function of the pancreas. Those who accept the theory of the glycogenic function of the liver, assume that normally the pancreas secretes a substance which is not discharged into the alimentary canal, but directly into the tissues (an internal secretion); this neutralises some other substance in the blood which inhibits or prevents sugar decomposition in the tissues, so that when the pancreas is removed this inhibitory substance is free, the sugar in the tissues is not split up and oxidised, and accumulates in the tissues. This explanation is probably incorrect, because the blood of a dog after extirpation of the pancreas, transfused into another dog, does not produce diabetes. Others again have assumed that the product of this internal secretion of the pancreas is a sugar-destroying ferment which passes into the circulation, so that after extirpation of the pancreas, sugar is no longer destroyed, and accumulates in the tissues; but this theory is also untenable, because ligature of the pancreatic veins does not produce diabetes. Furthermore, it must be remembered that some physiologists and pathologists, following Pavy, have abandoned the doctrine which gives to the liver a glycogenic function. Pavy believes that the liver, instead of forming sugar, prevents its entry into the general circulation, and thus secures escape from diabetes, and diabetes is therefore a failure or an impairment of the power of disposing of carbohydrate matter before the general circulation is reached. The exclusion of this special pancreatic secretion or product leads to a gross disturbance of the metabolism, and especially the carbohydrate metabolism, sugar and a number of other substances accumulate in the tissues, thus leading to a congeries of symptoms characteristic of acute and fatal diabetes. Here there is in fact a metabolic toxæmia, due to elimination or inadequacy of this special pancreatic function, which, like that of the thyroid gland, controls the mechanism of the normal metabolism. In either case, if the control disappears, incomplete or intermediate metabolic products find their way into the blood stream. Through the elimination of the pancreatic function the body becomes inundated with deleterious and incomplete products of its own metabolic activity, which normally are either absent or are present only in minimal quantity. They are in pancreatic diabetes accumulated in such amount, that they may be found in the blood and urine in abnormal quantities.

The results obtained in diabetes with administration of pancreatic substance are, however, in striking contrast to the brilliant success of the specific thyroid treatment of myxœdema. Experimentally, also, all attempts at removal of the diabetes produced by extirpation of the pancreas by means of implantation of pancreas have failed, although Minkowski succeeded by previous implantation in

preventing a pancreatic diabetes. Clinically, the administration of pancreatic substance has been practically useless, not only in cases of diabetes which were unaccompanied by pancreatic lesions, but also in typical cases of pancreatic diabetes.

Suprarenal glands.—In recent years the suprarenal bodies have been added to the list of those glands which possess an internal secretion.

Experimentally it has been proved that the suprarenal glands are vital organs; their complete removal causes death, though removal of one capsule only produces no ill effects. The injection of suprarenal extracts after complete extirpation delays death. The animals die with symptoms suggestive of intoxication, and the blood of an animal deprived of its suprarenal glands becomes toxic, not indeed to normal animals, but to animals whose capsules have been removed.

All this is highly suggestive of an analogy between the thyroid gland and the suprarenal capsules. More recently the physiological action of the suprarenal extract has been carefully studied by Oliver, and by Schäfer and his pupils, and they have shown that this extract, although fatal in large doses, in small doses possesses extraordinary powers as an arterio-constrictor, a cardiac tonic, and a muscular stimulant. It may be assumed, from these observations, that the suprarenal capsules secrete a useful stimulant substance, or that they are excretory organs, in which case the extract is a tissue poison. Accordingly, disease of the suprarenal capsules may lead to symptoms, either because the toxic influence of the secretion has been eliminated, or because certain poisonous substances are no longer excreted or neutralised and absorbed. It is striking that Addison's disease is almost always accompanied by caseous or tuberculous degeneration of the suprarenal capsules, whilst tumours, especially carcinoma, only rarely lead to Addison's disease. The exact relation of the suprarenal capsules to Addison's disease is as uncertain as that existing between diabetes and the liver and pancreas, but some such close connection there must be. It may be a toxæmia caused by the elimination of a specific function of the suprarenal capsule, which, as above explained, may be either secretory or excretory and antitoxic. If this function is antitoxic, then it may be that the capsules are capable of destroying certain intermediate and incomplete metabolic products carried through them by the blood; what these products are, it is impossible to say, although it may be noted that certain observers hold that the suprarenal capsules act upon neurin and render it harmless. This, however, has been strenuously denied.

Clinically, it may be said that Addison's disease resembles a toxæmia; there are always present severe cachexia, anæmia, and other serious disturbances of the general state of nutrition, and intense nervous phenomena, such as coma, delirium, and convulsions. It is possible that all these toxæmic symptoms may not be the primary consequences of suprarenal disease, but the secondary effects of a general disturbance such as may be observed in a cancerous cachexia, or of changes in the nervous system. It must be remembered that the specific treatment of Addison's disease by means of administration of suprarenal extracts, suggested by the above hypothesis of an internal secretion, has so far been useless, and certainly not specific. Amelioration of certain symptoms has been observed to follow the administration of suprarenal extract in some cases of Addison's disease, but never a cure; there is no evidence as yet of any specific effect in the least comparable to that observed in cases of myxœdema treated by means of thyroid substance.

The successful treatment of myxœdema by means of the administration of thyroid substance, and the suggestive experimental results obtained in animals

after ablation of the pancreas and suprarenal capsules, have established a new principle in therapeutics, which consists in the vicarious supply of certain active substances of which the body has been deprived either through functional or organic disease. Misled by this success, and beguiled by the enthusiasm of serious and sensational observers, physicians and surgeons have rushed to the use of tissue extracts of all sorts of organs for the treatment of various diseases and symptoms, displaying thereby an ignorance of physiological and pathological facts, and an absence of sound criticism, worthy of the Middle Ages. Cardin has been prepared for the treatment of cardiac weakness; nephrin for the treatment of renal atrophy; an extract of nerves, spinal cord, brain, and prostate, for diseases of the nerves, cord, brain, or prostate; and a physiologist has attempted to remove the weaknesses of his old age by using an extract of the organ largely associated with the manifestation of vital energy. It must be remembered, however, that destructive lesions which have produced permanent changes and an enduring loss of substance can never be made good. No amount of nervous tissue injected into the body can supply degenerated nervous substance, which perhaps has been replaced by fibrous tissue, whether this belongs to the central, peripheral, or sympathetic system. The specific organic treatment can only be successful where a functional loss of a specific secretion has to be dealt with, *i.e.*, there can be no hope of re-establishing the function of an organ structurally altered, which depends on its physical and anatomical structure. Thus, assuming that the kidney, as has been suggested, possesses an internal secretion, it is also known to possess an excretory function, which depends on its anatomical configuration. In atrophy of the kidney there would be impairment of its hypothetical secretory function, and of its actual excretory function. Injections of nephrin might replace the former, but what good could it possibly do in the re-establishment of the excretory powers? no amount of nephrin will transform fibrous tissue into renal tissue. The thyroid gland has a purely secretory function, and disease can do no more than impair this secretion; the conditions are quite different from those found in the kidney.

There is, however, another aspect of this question. The study of the various tissue extracts has demonstrated that some of them possess striking properties, and again the use of thyroid extract in myxœdema has revealed extraordinary powers of this remedy to remove certain morbid changes and symptoms. Soon, therefore, the question arose whether some of these substances might not be used as medicinal agents, not specifically to replace the functional loss of a specific secretion, but as a drug for the treatment of certain symptoms. Thus, having learnt that thyroid extract causes a rapid loss of weight in myxœdema, physicians have administered it with some measure of success in obesity. The action of the thyroid extract upon the skin of myxœdematous patients suggested the treatment of certain skin diseases, such as psoriasis and lupus, with the same remedy. The good effect upon the mental condition of myxœdema patients also led to its use in diseases of the mind. In many cases the thyroid extract has done good, although in others it was without effect; it may seem justifiable to adminster it under certain conditions, but not, perhaps, indiscriminately until the physiological action of the remedy is more fully understood.

In conclusion, then, it may be affirmed that recent observations and experiments have supplied physicians with another new method of treatment, namely, the administration of organic extracts. As in the case of the serum treatment, this may be—(1) *specific* (thyroid extracts in myxœdema and other diseases due to inadequacy of thyroid gland); (2) *non-specific*, when these tissue extracts are used like ordinary drugs to

allay certain symptoms or to produce certain effects (suprarenal extract as a vasomotor constrictor). If diseases due to functional loss of the specific thyroid secretion be excepted, the new specific treatment has not fulfilled those promises which the earlier observations aroused.

PREVENTIVE INOCULATION.

The principles of immunisation are also applied to the prevention of disease, especially of epidemic disease. Before the day of pathological bacteriology, Jenner had established protective inoculation by means of attenuated virus, more or less empirically, but none the less surely and consciously. In medicine, protective inoculations are used only to a limited extent, yet an acquaintance with what has already been done, or is being done, in this direction is necessary.

Inoculation with attenuated virus.—This is exemplified—By *vaccination against variola* with cowpox lymph, which must be regarded as attenuated smallpox virus. The success of vaccination is unquestionable, and though many problems regarding the nature of the virus yet remain to be solved, this much is certain, that though vaccination does not supply a life-long protection (what method of immunisation does?), smallpox runs a much milder course in those who have been vaccinated, and among them the mortality is considerably reduced. Thus, according to Koch's statistics, of 27,794 non-vaccinated smallpox patients, 32 per cent. died; while of 181,000 vaccinated ones, 9·5 per cent. died; and of 6015 revaccinated ones, only 7·4 per cent. In the case of vaccinia the attenuation is produced by passage through the animal body.

For *hydrophobia* Pasteur practised another method of attenuation. The virus of this disease is as little known as that of smallpox, yet the French master showed that by drying the virus of rabies, contained in full power in the spinal cords of rabbits, it can be weakened to almost any desired degree, and then used for the purpose of vaccination. It may be used even during the long incubation period that occurs after infection. The mortality from hydrophobia has been considerably reduced by this prophylactic treatment, and with improvements in the methods the mortality has steadily decreased from 0·94 per cent. in 1886 to 0·32 per cent. in 1890.

In the protection against smallpox and rabies, materials are used that are taken directly from the animal body, and of the virus itself nothing certain is known. The principle has of late years been extended by Haffkine in his anticholeraic vaccination.

Inoculation with dead or living pure cultures.—Haffkine originally used an inoculation *in cholera* of attenuated living cultures of cholera vibrios as his first vaccine, which was then followed by an inoculation of highly virulent cholera vibrios, used as a second vaccine. This method has been modified by him in course of time, so that at present only unaltered virus is used, but his original method was essentially the same in principle as that practised in the case of anthrax. His results have been highly satisfactory. Thus in Calcutta Haffkine found that the mortality among the inoculated was 17·24 times less, and the incidence of cholera 19·27 times less than among the non-inoculated; evidence certainly in favour of the anticholeraic vaccination. This evidence has recently become still stronger through the researches of Koch, who has shown that, as the result of Haffkine's method

of vaccination, the bactericidal power of human serum grew 3500-fold, and that after a year it was still twenty times as great as that of normal serum.

It has been attempted or suggested to protect persons against *plague or enteric fever* by using sterilised cultures of the plague or typhoid bacillus respectively, administering the material by subcutaneous inoculation. In both cases the results have been promising, but more actual evidence of the value of the method is still wanted. It is reasonable and also humane in times of epidemics to practise, along with all possible general measures, such preventive inoculations as are based upon sound laboratory experiments; which, properly carried out, can do no harm beyond giving slight temporary and local inconvenience.

Inoculation with antitoxic serum.—The previously mentioned methods are all instances of active specific immunisation, but the principle of passive specific protection by means of immunising serum has also been applied, notably in the prophylaxis against diphtheria. Here it is recommended to inject 150–250 units. The statistics reported by Dr. Hermann Biggs are in favour of the use of these preventive inoculations for the purpose of protecting a household or a community. Although it may be difficult to gain absolute certainty, Dr. Biggs writes that by the use of diphtheria antitoxine in four great institutions for children in New York, in which diphtheria was prevailing in epidemic form, it has been possible to completely stamp out the disease. Serious results have never resulted from the injections, but the immunity only lasts for from two to four weeks. With regard to tetanus, preventive inoculations with antitoxine have, according to Nocard, been successful in horses; but in man the few observations recorded do not seem promising, probably because of the transitory nature of the passive immunity and the uncertainty of an existing infection. Nevertheless, these methods of passive immunisation where occasion arises for their use are worthy of all consideration, especially if the patient can be treated as soon as he is wounded or bruised.

<div align="right">(A. A. KANTHACK.)</div>

[The late Professor Kanthack was engaged on this article at the time of his death. Certain parts were completed; others had been drafted but had not been arranged and filled in; of others, again, there were but rough notes. The completed portion, especially that dealing with inflammation and repair, has been left unaltered (except that it has been condensed), and represents his latest opinions on these subjects. Throughout the article an attempt has been made to reproduce from his numerous papers and the recollections of certain of his friends any special views that he held. For portions of the work to which Professor Kanthack had paid no special attention, or on which he left no full notes, or none at all, I must hold myself responsible.

<div align="right">G. SIMS WOODHEAD.]</div>

SECTION I.

GENERAL DISEASES.

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TYPHUS FEVER.

Syn., Fr., *Typhus exanthématique ;* Ger., *Fleckfieber.*

AN acute specific infectious fever, prevailing in epidemics and usually associated with conditions of overcrowding and destitution. Characterised by a sudden onset, a petechial rash, marked nervous symptoms, with great mental confusion and physical prostration, and by a rapid defervescence on or about the fourteenth day.

History.—There is very little doubt that this disease has been known from the earliest times. It is highly probable that typhus was the epidemic which ravaged Athens, as described by Thucydides. We may also assume that typhus fever was the disease which so frequently broke out in camps and armies in the Middle Ages. No doubt a proportion of such cases were typhoid, as it is only comparatively recently that these two fevers have been recognised as distinct from one another. But the conditions under which these epidemics arose were undoubtedly such as to favour the outbreak of typhus. Indeed, "camp fever" is one of the many names which have been given to it. It has also merited the name of "jail fever," as in the seventeenth and eighteenth centuries it repeatedly broke out and spread with frightful rapidity in the overcrowded prisons in this country. Although very many observers before him had rendered full accounts of typhus, and had distinguished it from both typhoid and relapsing fevers, it is to Murchison we are indebted for the best description hitherto given of the disease.

As regards *geographical range*, typhus has at different periods been seen all over Europe. It is uncommon in the tropics, and it is suggested that the conditions of life in temperate climates, where during the winter people are more likely to crowd together to avoid cold, are more favourable to its development. The two countries which have suffered most from it in this century are Russia and Great Britain ; and although modern sanitation has made a great epidemic in this country almost impossible, still small outbreaks do occur occasionally. Ireland has long had an unenviable notoriety for the prevalence of the disease, and it has been said to be endemic in the narrow closes of the Old Town of Edinburgh. The latter

statement is not justifiable, as, though outbreaks occasionally do occur, they can nearly always be traced to importation from an outside source.

Etiology.—That the *exciting cause* of typhus is a micro-organism of some description, there can be no reasonable doubt, but hitherto it has not been discovered. Thoinot and Calmette have described bodies resembling human spermatozoa in the blood of typhus patients, but their observations have never been confirmed. Hlava of Prague described a streptobacillus in 1891, but his work also requires proof. Dubief and Bruhl made a bacteriological research into some cases which occurred in the prisons of Paris in 1893. They found post-mortem a diplococcus in the lungs and bronchial secretion. Lastly, Balfour and Porter, during a recent outbreak in Edinburgh, described a diplococcus which differed in many respects from that of the French observers. It was found both post-mortem and in the blood during life. It is too early, however, at present to claim the micro-organism they have discovered with any confidence as the cause of the disease. The possibility of the origin of typhus *de novo* is not now admitted.

The *predisposing causes* of typhus are overcrowding and conditions which lead to overcrowding. Starvation is also said to predispose, and obviously such a contagious disease would spread more rapidly in periods of famine, when the resisting power of the population is lowered. But if half-starved people lived under favourable sanitary conditions, there is no reason to believe that the disease could spread. In regard to season as a predisposing cause, it is in the winter months that typhus is most common, since it is at that time windows are kept shut and the poor huddle together for warmth. Mental and physical fatigue and ill health may also be regarded as secondary predisposing causes.

Dissemination.—Typhus fever is directly contagious from person to person. Nurses from their close attention on patients are very liable to take it. Physicians also, especially if they attend the patients in their own homes, run a considerable risk. In hospitals, however, if sufficient attention is paid to free ventilation, accidents of this kind are uncommon. It would seem, indeed, that a certain concentration of the poison is necessary to cause infection, and that the unknown germ of the disease cannot exist in fresh air. The "striking distance" of typhus is a very short one. It is probably necessary to be in absolute contact with the patient or to enter an unventilated room in which a patient is lying. Harvey Littlejohn, in investigating the spread of the last outbreak in Edinburgh, proved conclusively that, even in large overcrowded tenements where several families occupied different rooms on the same flat, the disease did not spread from one family to another unless they were in the habit of entering each other's rooms. The people who were not on intimate terms with the infected families escaped, although their rooms opened into the same narrow and imperfectly ventilated landing. The poison, however, susceptible as it is to fresh air, can retain its virulence for a long time in houses that have not been disinfected or thoroughly aired. Old clothes and bedding have been on more than one occasion the cause of an outbreak, and the mere handling of them to prepare them for disinfection has given sanitary officials the disease.

Morbid anatomy.—Typhus cannot be said to have any characteristic post-mortem appearance. Decomposition sets in early, and the autopsy should be made as soon as possible. All the internal organs are, as a rule, congested, and sometimes small hæmorrhages may be seen on

their surfaces. The heart's substance is soft and friable, and its cavities are somewhat dilated. The myocardium presents the characters of an acute parenchymatous degeneration. Microscopically, the muscular fibres show cloudy swelling, along with loss of striation and the presence of fat granules. The blood is dark and fluid. The lungs show great hypostatic congestion, often with consolidation at the base. The spleen is enlarged, very soft, and occasionally diffluent. The membranes of the brain are congested, and the lateral ventricles are often distended with fluid. The intestine shows no internal ulceration, though occasionally small ulcers have been seen in the stomach. There is then no sign by which the disease can be recognised after death, though of course the existence of genuine petechiæ on the skin, with the appearance detailed above, would afford a strong presumption that the case was one of typhus.

Symptoms and course.—The *period of incubation* appears in most cases to be about twelve days. It is often a matter of difficulty to determine this period accurately, but it would seem rarely to exceed that time. Not a few instances are on record where a much shorter incubation appeared probable. During this period there are no well-defined symptoms.

This fever being one of a fortnight's duration, it will be convenient in a general description to consider the symptoms as presented during each of the two weeks of its progress.
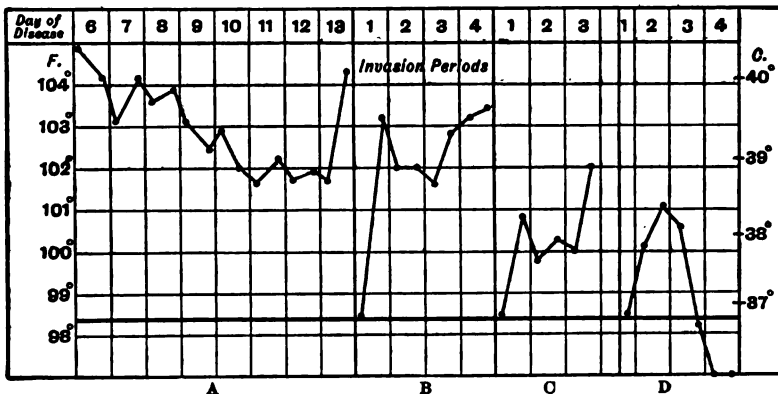
Fig. 1.—A, Fatal case of typhus in a male adult; B, C, and D, Examples of the temperature curve during the period of invasion.

THE EVENTS OF THE FIRST WEEK.—The *invasion* of typhus fever is on the whole pretty well marked, thus differing from that of typhoid. A rigor, but perhaps more frequently sensations of chilliness, distinct and recurring, usher in the attack. The onset is followed by headache, which is a very constant symptom. It is frontal for the most part, and is usually severe, sometimes agonising. Pains in the back and limbs, or soreness all over, are also present, and there is restlessness and disturbed sleep. The temperature rises to a high point (102° to 103°) from the first day, and continues to rise for several days, while there is little or no morning remission; the pulse is frequent and full, and the respirations are increased in rate. A sense of prostration is a prominent symptom from the outset, and the patient is compelled to take to bed. The face is flushed, the eyes red, the pupils somewhat contracted, and there is photophobia. The tongue is at first thickly coated, but it soon becomes dry, and there is thirst, loss of appetite, and constipation.

These various symptoms may readily be mistaken for some other febrile affection during the few days of their continuance, but soon the more characteristic features of the fever declare themselves. On the fourth or fifth day there usually appears the *eruption of typhus.* It consists of spots of irregular size (from 1 to 3 or 4 lines in diameter), of pale pink colour, with ill-defined edges, slightly raised above the skin, and at first disappearing on pressure. The spots are isolated or gathered in groups, and are first seen about the anterior folds of the axillæ, on the backs of the hands and of the elbows, and then upon the chest, abdomen, and flanks; but they soon spread more or less over the whole body and limbs. They are not so noticeable, although they are often present, on the face. In addition to these spots, there is an irregularly congested condition of the skin, giving to it a somewhat marbled appearance (subcuticular mottling). The spots, which have at first a certain resemblance to a fading measles eruption, tend to become darker in colour, and acquire an appearance a little suggestive of flea-bites, all the more so that in the centre of some of them may be observed a slightly darker point—a minute extravasation; but their want of definition at the margins is an important distinction.
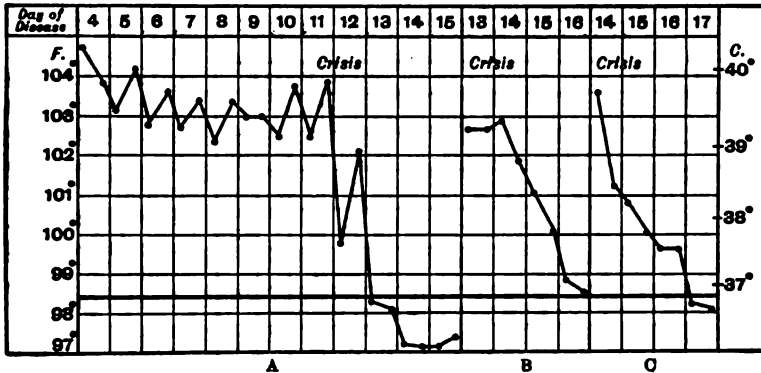
Fig. 2.—A, A case of typhus in a young adult; B and C, Examples of termination by crisis.

The spots and the mottling together constitute what is termed by Sir William Jenner the " mulberry rash " of typhus. Although in some cases this rash is so small in amount as to be with difficulty detected, it is extremely seldom absent, except in young children. The later days of the first week are marked by an increase in the febrile symptoms and by advancing prostration of strength. The temperature continues high (103° to 105°); the pulse becomes more frequent and feeble; the tongue is dry and brown, and sordes accumulate on the teeth. The urine is scanty and high-coloured, and often contains a little albumin. The breath and the body exhale a peculiar odour, which has been held by some to possess diagnostic importance. The patient now has a dull, heavy, dusky aspect. He complains less of headache, and is somewhat drowsy, but can easily be roused when spoken to loudly, for there is some dulness of hearing. Delirium may be present, particularly at night.

THE EVENTS OF THE SECOND WEEK.—The symptoms now assume a character more truly typical of this fever. The patient becomes utterly prostrate, and insensible to everything around him and to his own wants. He lies low in bed with his eyes closed, and the appearance of being in a

deep sleep or stupor from which he cannot be fully roused, although in general he can be persuaded to take food. His face is darkly congested, or more rarely pallid, and his breathing is frequent and audible. Delirium, usually of a quiet muttering character, is present. Occasionally it is busy, noisy, or violent. The hands are moved aimlessly about or pick at the bedclothes, while the tremors of the muscles and subsultus tendinum indicate the great nervous and muscular weakness to which the patient is reduced. The temperature may have slightly subsided after the sixth day, but it still continues high, and the pulse becomes more rapid (120 to 130) and feeble. There is usually retention of urine. For several days the patient may remain in this condition without much change, or again the symptoms may advance, and death ensue from sheer exhaustion or from deepening coma, accompanied with pulmonary engorgement. Occasionally, sudden heart failure precipitates the end.

In most cases, however, a favourable change begins to show itself about the end of the second week (usually the fourteenth day), when there occurs the phenomenon of the *crisis* which forms so striking a feature in the clinical history of a case of typhus. The temperature falls rapidly, often reaching the normal point in less than twelve hours; the pulse becomes slower and better in character; a gentle moisture appears on the skin, and the patient seems to be in a more natural sleep, from which he awakes looking much brighter. This change in the face is very significant of the crisis. The tongue can now be more readily protruded, and is moist at the edges. The urine is more abundant, and is loaded
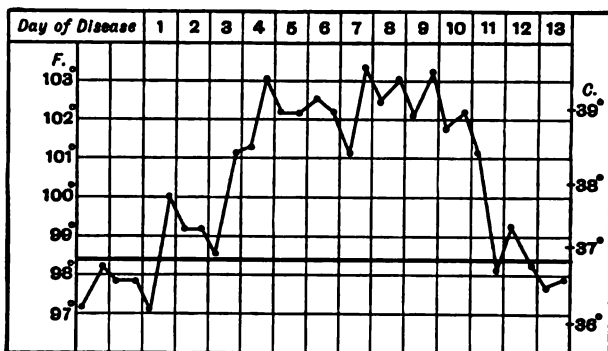
FIG. 3.—Complete course of typhus in a child, æt. 4.

with urates. The patient shows signs of returning consciousness, although there may still be some delirium and confusion. Notwithstanding a feeling of extreme weakness, convalescence is soon established, and proceeds rapidly, being rarely interrupted; as a rule, recovery is complete in three or four weeks after the crisis.

The patient may have no recollection of his illness, or it may be in his memory as a vague dream. Sometimes he imagines himself to have been away on a long journey, and is able to recall its incidents. Occasionally, on the other hand, his fancies have been of a distressing or agonising character, the memory of which remains even long after recovery.

Analysis of some of the chief symptoms, including complications.— *The febrile symptoms.*—The temperature rises rapidly from the onset of the attack, and even on the first day may be 102° or 103°. It continues rising slightly during the greater part of the first week, by the end of which it has usually attained its maximum point, which in an average case rarely exceeds 105°, except in the case of children, in whom it may be higher. There is very slight if any morning remission. In the second week of the fever the temperature may show a ·slightly lower level,

but it still continues high until about the twelfth or thirteenth day, when it begins to move a little either in the upward or downward direction. This occurs prior to the crisis, which, as already mentioned, is recognised partly by the rapid descent of the temperature to normal.

A very high temperature (over 105°) in the first week, especially if accompanied, as it often is, with head symptoms, marks a severe and anxious case, and the same may be said of those attacks in which the temperature of the second week exceeds that of the first. The temperature, however, is not an absolutely reliable indication of the severity of a case, but must be considered along with the pulse and other symptoms, particularly those relating to the nervous system. Thus a case may show no unusual course of the temperature, and yet be of most unfavourable prognosis, owing to its adynamic character, the pulse being small and frequent, and the delirium and prostration very pronounced. Hyperpyrexia is rarely met with in this fever, although in fatal cases there may be a swift rise of temperature to a very high point shortly before death. Complications may influence the course of the temperature, and render it less typical of the fever. In some instances, particularly among children, defervescence may take place by lysis, and the case go on for sixteen or

FIG. 4.—A, Complete course of typhus in a woman, æt. 67 ; B, Rare instance of termination by lysis.

more days before the normal temperature is reached. Afebrile cases of typhus have on rare occasions been met with. Sometimes a final crisis occurs at the end of the first or beginning of the second week.

Circulatory System.—The pulse is quickened from the first (100 to 120), thus presenting a contrast to typhoid fever, in which it is often comparatively infrequent at this period. But the relation of pulse and temperature is not absolute in typhus. At the outset the pulse is full and soft, but it soon loses this character, becoming small and frequent, particularly during the second week, when low tension and dicrotism are often marked. A pulse rate over 120 in an adult generally indicates an anxious case, and where it exceeds 130 the mortality is very high. Unsteadiness or irregularity of the pulse, as the fever approaches the crisis, is often of evil omen. Cases of unusually rare pulse have been observed by Murchison, Maclagan, and others, in which the rate was below 40 or even below 30. In some of these cases the infrequency continued only for a few days; in others there was a want of synchronism between the radial and cardiac pulse rate, the former showing only one pulsation for two of the latter. Unusually rare pulses generally testify to marked cardiac weakness, and the prognosis in such cases is not favourable.

After the crisis is past the pulse may subside to a very low rate, and while such a condition is generally only temporary, it is not without its risks, and requires while it lasts special care, particularly as regards exertion on the part of the patient.

The physical examination of the heart is of great importance. In most cases, as the fever advances and the heart's action becomes more rapid, a diminution in the force of the cardiac impulse is perceptible, and the first sound at the apex becomes less clear, or almost inaudible, the second sound being by contrast sharp and distinct. A soft blowing murmur may occasionally be heard at the apex. The cardiac condition during the progress of the fever claims the special attention of the physician, as, owing to the changes which affect the myocardium, heart failure is a danger to be feared.

Respiratory System.—The respiration is more or less increased in frequency in typhus as in all fevers. In mild cases this increase may not be very great, but in general during the second week a marked acceleration takes place, the rate rising to 30, 40, 50, or more. The breathing is short, shallow, and audible. When insensibility comes on, a puffing or hissing character of the respiration may be observed, as in comatose conditions, with increasing duskiness of the face. Marked irregularity of respiration is an unfavourable sign.

Some amount of bronchial catarrh is very common, and shows itself by slight cough and by the presence of sonorous and sibilant sounds all over the chest. Hypostatic congestion of the lungs, while probably present to a certain extent in all cases, frequently assumes the character of a dangerous complication. Depending in great measure upon the increasing cardiac weakness, it may also be predisposed to by the shallow character of the febrile breathing already described, and by the decubitus of the patient. It is most apt to be present during the second week of the fever. It reveals itself by quickened breathing, cyanosis, and feeble cardiac action. Cough may or may not be present. The physical examination shows evidence of pulmonary engorgement and œdema, by the impaired percussion note at the bases of the lungs or all over posteriorly, together with faintness of the vesicular breathing, and the presence of medium crepitating râles and sonorous and sibilant rhonchi. In not a few instances this complication has a large share in bringing about a fatal result.

True pneumonia rarely accompanies typhus fever, but when it does occur it is a grave complication, both in itself and from the risk of gangrene of the lung. Laryngitis is an occasional complication of typhus, and is always to be regarded with anxiety, from the danger of acute œdema glottidis.

Alimentary System.—The tongue is at first moist and covered with a thick fur, and in mild cases may remain in this condition throughout. Usually, however, by the end of the first week it has become small, rough-looking, dry, and covered with a brown and cracked incrustation. The condition of the tongue, together with the increasing apathy and deafness of the patient, renders its protrusion difficult, so that it is not always possible to obtain a good view of it. Sordes accumulate on the teeth and lips as well as the tongue, particularly during the second week, and impart a dark appearance to the mouth.

Thirst is a prominent symptom at the beginning, but later on is not complained of, although as a rule the patient readily takes liquids. There

is loss of appetite from the first, but after the crisis it speedily returns and as a rule is a good sign of convalescence. Gastric irritation in the form of vomiting is an occasional occurrence, but it rarely continues long. It sometimes ushers in a severe case. The intestinal symptoms are not marked in typhus. Constipation is the rule, although sometimes the bowels act quite naturally. Diarrhœa is very rare, but it sometimes occurs at the time of the crisis. There is little abdominal pain or swelling, but occasionally there is tenderness on pressure in the right hypochondrium. Both liver and spleen are slightly enlarged.

Urinary System.—The urine is at first reduced in amount and dark in colour. Its specific gravity is higher than normal (1025 to 1030). In the later stages of the fever the urine often returns to its normal character, although there is very frequently retention, necessitating the use of the catheter. On the occurrence of the crisis it contains a large quantity of urates.

The proportion of urea is largely increased during the first week of the fever. In the second week it may still continue high, but in some cases it is found to have fallen to the normal amount or even below it. It seems not improbable that in such instances its elimination is insufficient. About the time of the crisis the amount of urea may again become increased, but when convalescence is established it gradually returns to its normal proportion.

Symptoms of uræmia may arise in the course of typhus, and the danger of this is greatest where the urine is greatly diminished or suppressed. It has been suggested by Murchison and other observers, that the head symptoms of typhus may be largely due to uræmia rather than to any inflammatory or congestive condition of the brain and its membranes. The uric acid is increased. The chlorides are diminished or absent during the progress of the fever, but return when convalescence sets in.

Albumin is present in greater or less amount in a large proportion of the cases of typhus. It is usually of so-called febrile character, disappearing after the crisis. But it would appear in not a few instances to be due to an accompanying complication of acute nephritis, as proved by the presence of blood and of tube casts in the urine, as well as by post-mortem evidence. In a considerable number of cases of typhus the urine gives the "diazo" reaction, thus proving the unreliability of this test as diagnostic of typhoid fever.

Nervous System.—Headache is one of the most important and constant of the earlier symptoms of typhus fever. It is rarely absent, but it differs as regards severity in different cases. In a large number it is moderate, but continuous and depressing. In a few, and especially among the young, it is agonising. It is most commonly frontal, but it may be temporal, occipital, or referred to the whole cranial region. The patient's facial expression often bears testimony to the severity of the headache, in the wrinkled brows and the extreme sensitiveness to light or noise. Giddiness is a common accompaniment of the headache, and is especially felt in sitting up. Pains in the back and limbs, and a sense of weariness, are often among the early symptoms. About the end of the first week, the patient's nervous symptoms undergo a change. He complains less of headache, and becomes dull, apathetic, and drowsy. His intelligence is blunted, and he is slow in comprehending and in responding to questions, his answers being at the same time confused. His memory, too, is impaired, and he may not be able to remember anything about his illness,

or to tell where he is. He is less alive to his wants, and seems to prefer to be left undisturbed. During the night he is wakeful and more or less delirious. It is, however, mostly during the course of the second week that the characteristic nervous symptoms of typhus become prominent. There is now delirium both by day and night, although its degree varies greatly, much depending upon the severity of the case, as well as upon the patient's temperament, habits, and occupation. Sometimes it is of a quiet muttering and not unhappy form; at others, busy and talkative, not unlike delirium tremens. Occasionally it is wild and maniacal (delirium ferox); and in this condition, which is one of grave danger, errors in diagnosis have sometimes been committed. Deep coma, also a symptom of gravity, may occur in the course of the second week, as may also the state of *coma vigil,* described by Sir William Jenner, in which the patient, although quite insensible, lies with his eyes widely open, with pale face, clammy skin, rapid and feeble breathing, and an almost imperceptible pulse. This condition is said to be invariably fatal, yet it must be admitted that cases do occur in which many of these symptoms present themselves, and where, notwithstanding, recovery takes place.

The effects of typhus fever upon the nervous system are further illustrated by the patient's extreme prostration, as shown by the low dorsal decubitus, the trembling of the muscles and subsultus tendinum, which are seen as the disease advances in the second week, as also by retention or incontinence of urine or fæces.

Various other nervous symptoms are of occasional but rare occurrence, such as convulsions, muscular rigidity, and cutaneous anæsthesia or hyperæsthesia. Cerebral meningitis is sometimes met with in typhus fever, and has been a prominent feature in some of the recorded epidemics.

The organs of special sense rarely suffer to any serious extent. The condition of the pupils has already been referred to. They are contracted during the greater part of the fever, and they may also be unequal. In profound coma the pupils may present the pin-hole appearance described by Graves, but, on the other hand, dilatation of the pupil has occasionally been observed in this condition. The hearing is impaired after the first few days, and this may continue on to the convalescence, when it gradually passes off. Although it has been stated to be a rather favourable symptom, it is only relatively so, and would really seem to have little prognostic significance. Otitis media may occasionally be met with in this fever.

Sequelæ.—Numerous sequelæ, more or less common to all forms of blood poisoning, are to be met with in typhus fever. Among these may be mentioned pneumonia, pleurisy, and empyema, pyæmia, noma, boils, abscesses, and tuberculosis. Only the more important and characteristic will be referred to.

Swelled leg is an occasional sequel of typhus, generally occurring in the convalescence while the patient is still in bed. It is preceded by pain in the calf of the leg, usually the left leg, which soon becomes swollen and stiff, and the whole limb attains an enormous size, and is pale and glazed-looking. It is due in most cases to thrombosis affecting the femoral vein, which may be felt to be hard and painful; but it would seem in some instances to depend upon an obstructed condition of the lymphatics or to inflammation of the areolar tissue. It is not generally attended by much constitutional disturbance, and it tends to pass off completely in the course of a few weeks. In some cases, however, the limb may long continue to

feel weak, and its veins become varicose. Arterial thrombosis leading to gangrene is very rare.

Glandular swellings and affections of the skin.—Inflammatory swellings of the parotid and submaxillary glands occasionally occur about the time of the crisis, or in convalescence. They usually affect one side of the face, but may involve both. The swelling forms rapidly, and may attain to a large size, causing pain and discomfort in attempting to open the mouth. There is much constitutional disturbance and prostration. Not infrequently suppuration takes place and an abscess forms, but, on the other hand, the swelling may disappear spontaneously. Similar swellings may occur in the inguinal and other glands, forming buboes; or, again, there may be cellular tissue abscesses in various parts of the skin. These glandular affections have suggested the strong resemblance of typhus fever to bubonic plague, and Murchison seemed to regard the two diseases as probably identical—a view, however, which can hardly be maintained at the present day.

Nervous sequelæ.—Certain forms of paralysis may sometimes be met with in the convalescence from typhus. Of these the most frequent is hemiplegia, with or without aphasia. The lower extremities may be paralysed, and present some of the symptoms of a peripheral neuritis. In most cases the paralysis passes off, but in a few it remains permanently.

Affections of the mind may show themselves after the febrile symptoms have passed off, usually in the way of mental weakness and loss of memory, imbecility, melancholia, or, in rare instances, sudden maniacal attacks. In these mental sequelæ of typhus the prognosis is, as a rule, good.

Varieties of typhus fever.—Numerous varieties have been described, but it is seldom possible to draw sharp distinctions, except to the extent that in some cases certain of the features of this fever assume a more marked prominence than in others.

The following are among the varieties described by Barrallier, Murchison, and other authorities:—

Inflammatory typhus, in which there is high fever, flushing of the skin, severe headache, and acute delirium. Such cases occur mostly in the young and robust, and in persons of the upper class.

Nervous or ataxic typhus (brain fever).—Cases in which the nervous symptoms of delirium, somnolence, tremor, etc., predominate, and the rash is usually dark and petechial.

Adynamic typhus.—Marked by great physical prostration, involuntary evacuation, and tendency to collapse.

Ataxo-adynamic typhus.—A combination of the two latter varieties; by far the most common form.

Typhus siderans.—A very severe and rapidly fatal form.

Typhus levissimus.—Where all the symptoms are of the mildest.

Catarrhal typhus.—So called from its frequent complication with bronchial and other chest symptoms. This form has been specially observed in Ireland.

Scorbutic typhus.—A grave form, in which hæmorrhages, both subcutaneous and internal, occur along with the fever. Some epidemics have been characterised by the prevalence of this form.

Diagnosis.—During the existence of an epidemic this is not difficult. When, however, there is no typhus in the neighbourhood, a first case may give considerable trouble, if it is not well marked. In children also, even where there is a history of exposure, it may be difficult to come to

a conclusion. The following are the chief points to which attention should be directed:—

The patient's general appearance and his mental condition are of importance. A flushed face with a "drunken" expression, and pink ferrety eyes, are suggestive of typhus. If added to this there is mental confusion and deafness, the presumption is strengthened. The presence of the rash is of course final, if it is well developed, but unfortunately it is occasionally absent altogether (especially in children), or may consist merely of the faint subcuticular mottling, which it requires a little practice to recognise. It should be looked for in the axillæ and groins, and is best seen in the shadow of the bedclothes, being often imperceptible in a strong light. Flea-bites may cause difficulty, but may be distinguished from typhus petechiæ by their well-defined outline as well as by the tiny puncture in their centre. To those who have had previous experience of the fever, its characteristic odour, if present, will give great assistance in diagnosis.

In coming to a conclusion, all other possibilities should be carefully excluded. The lungs, especially their apices, should be examined for *pneumonia,* as a typhoid condition in that disease may readily be mistaken for typhus. The other diseases to be differentiated are the following:—

Typhoid fever.—A full account of the differential diagnosis of this fever from typhus will be found in the article headed "Typhoid Fever."

Purpura. — The skin condition has been mistaken for a typhus eruption, but the hæmorrhages áre, as a rule, larger than in typhus, and there is no subjacent rash. Moreover, it is exceptional to find purpura associated with an elevated temperature, while the hæmorrhages from the mucous membranes so characteristic of this disease are rarely found in typhus. It is, however, to be remembered that there is a scorbutic or purpuric form of typhus.

Meningitis.—The absence of a rash is the chief distinction. Again, in meningitis the senses are at first preternaturally acute, whereas in typhus they are dulled. The typhus patient, therefore, is not nearly so irritable, nor is he so liable to utter the cerebral cry so characteristic of children with meningitis. On the other hand, it must be admitted that squint, ptosis, inequality of the pupils, and the like, though more frequent in meningitis, have all been noticed in uncomplicated typhus. The *tache cérébrale* may be of some assistance in making the diagnosis in favour of the brain condition.

Uræmia has been frequently confused with typhus, especially when supervening suddenly in a chronic kidney condition. The absence of rash and pyrexia should clear up the case, but it is as well during a typhus epidemic to remember that the mistake has been made.

Measles.—A fading measles rash occasionally very closely resembles that of typhus. The history of catarrh and of a profuse rash on the face will decide the diagnosis in favour of measles. The typhus rash does not usually invade the face to any marked extent, though it occasionally appears over the angles of the jaws. When the measles rash is well out on the body, and has not begun to fade, there should be no difficulty, the spots being more raised and larger than in typhus, while they are, moreover, often arranged in crescents.

Prognosis.—It may be broadly stated that the older the patient is the worse is his chance of recovery. The death rate varies considerably, but in many epidemics, when all cases, including children, are reckoned, it

is probably not much more than 10 per cent. If, however, only patients of over thirty years of age were counted, this rate would be probably at least trebled.

Any condition which has lowered the resisting power, or has impaired the organs of elimination, makes the prognosis very grave. Thus over-work, especially mental overwork, increases the chance of a fatal termina-tion. Alcoholism, above all, when it has permanently damaged the kidneys, gives the case an unfavourable bias. As regards symptoms arising in the course of the fever, which are of grave import, great nervous prostration in the early days of the disease is a very bad sign. The same may be said of delirium ferox, which is very exhausting to the patient. Coma occurring at any time is serious. A temperature rising rather than falling after the twelfth day is dangerous, and if about the fourteenth day it shows signs of rising above 106°, it is exceedingly probable that a fatal hyperpyrexia will terminate the case. Other very grave signs are flapping of the alæ nasi, hypostatic staining of the skin of the back, incontinence or retention of urine, and eyes with pin-hole pupils. Children, as a rule, go through the fever very well. On the other hand, heavy, fat persons, and very muscular and powerful men, often succumb.

Treatment.—Bearing in mind the fact that typhus is due originally to want of sufficient ventilation, it seems only reasonable to suppose that cases should benefit if nursed in large and airy rooms. In the plans of the new fever hospital for Edinburgh this has been recognised, and allowance is made for 3000 cubic feet of air per patient, a considerably larger figure than that suggested for the other wards. If this space cannot be provided, care should be taken to secure very frequent renewal of air, and indeed cases seem to do very well in what might be described as a draught. While the temperature remains high, the bedclothes should be very light, a single sheet and blanket being quite sufficient. After the crisis, however, it is advisable to move the patients to a convalescent ward kept at a warmer temperature, and to add an extra blanket to their coverings.

Typhus fever requires skilled nursing, and if a nurse who has had experience of it cannot be procured, it is well to get one who has at least had experience of nursing cases of typhoid fever. The patient's mouth should be most carefully attended to, and cleansed several times a day, the sordes being removed from the teeth and the tongue scrubbed and anointed with some antiseptic ointment, boric acid and vaseline being a good preparation. The patient should be sponged with a dilute antiseptic at least twice daily, or more often if the case is severe and the odour well marked. In the Edinburgh City Hospital, Jeyes' fluid is used for this purpose in tepid water. Great care should be taken to see that the patient has an opportunity of passing water frequently, and the bladder must be regularly percussed to see that no accumulation occurs. The patient should be abundantly supplied with cold water to drink. If he is too ill to ask for it, it should be forced upon him. The more fluid he takes the better is his chance of eliminating the toxines of the disease.

As regards diet, it must be remembered that though the bowel is not ulcerated, as it is in typhoid fever, still the high temperature renders the digestion exceedingly weak. The food must be fluid, and should consist chiefly of measured quantities, say 3 oz. of milk administered every two hours. The milk should not be allowed to stand at the bedside, but should be regarded as a meal. It may be supplemented by beef- or chicken-tea, fluid meat extracts, and egg-flip. After the crisis the

appetite rapidly returns, and this dietary may be increased by the addition of bread, fish, and chicken.

The question of stimulation is always important. It is not by any means necessary to give alcohol as a routine. If, however, the medical attendant is in doubt, it is safer to give it. Beef-tea will in many cases be quite sufficient to stimulate the patient. It must be confessed, however, that the majority of patients require alcohol at the time of the crisis, if they have not done so earlier. If, as happens especially in alcoholic cases, the stimulant fails to improve the pulse sufficiently, cardiac tonics, such as digitalis or strophanthus, may be of service. In cases where there is no diarrhœa, and where there is no subsultus, strychnine may be used with advantage. We may add here, that if alcohol is given, it must be given cautiously at first and in measured quantities.

Sleeplessness and excitement must be treated by suitable hypnotics. Beef-tea given hot is sometimes quite sufficient. If it is not, sulphonal, or, when the pulse is very bad, paraldehyde gives good results. If a hypnotic is given, it should be persevered with, and a second dose should be ordered if the patient is not asleep within the time the medicine might reasonably be expected to act.

Constipation and diarrhœa may both give trouble. For the former it is as well to remember that too large a dose of aperient medicine may cause a troublesome attack of the latter. Enemata are therefore to be preferred, or very small, say 1-drm., doses of castor-oil. For diarrhœa, it is first necessary to stop the beef-tea or any meat preparation which the patient is taking, and either to boil the milk or dilute it with lime-water. Occasionally an astringent may be required.

Headache is often a distressing symptom. A 5-gr. powder of citrate of caffeine may relieve it, and is preferable to any drug of the phenazone group. Evaporating lotions or ice to the head may also be of assistance.

For coma, strong coffee has been recommended. Blisters have also been used, but they are not without disadvantages. However, in desperate cases their use is quite justifiable.

If there is retention of urine, the water should be drawn off regularly with a catheter.

Prophylaxis.—The pulling down of old houses, the opening up of slums, and the prohibition of one-roomed dwellings, are the most rational measures for preventing the outbreak of typhus. If the outbreak has occurred, the compulsory isolation in hospital of the sufferers, and quarantine of those exposed, will do much to stamp it out. In hospital, airy wards and strict attention to personal hygiene on the part of nurses and doctors, reduce the danger to a minimum.

The typhus patient is free from infection five weeks from the onset of the disease. His clothes, if not destroyed, should be carefully disinfected by steam before he is allowed to leave hospital.

J. O. AFFLECK.
CLAUDE B. KER.

RELAPSING FEVER.

Syn., FAMINE FEVER; SPIRILLUM FEVER (Fr., *Fièvre à rechute;* Typhus *récurrent;* Ger., *Armentyphus*).

AN acute infectious fever, characterised by the presence of a spiral micro-organism in the blood, by a rapid onset and defervescence, and by a repetition of the fever after a week's apyrexia.

History.—Relapsing fever was first accurately described by Rutty as occurring in Dublin in 1739. There is, however, little doubt that it existed previously, and indeed Murchison has identified it with a disease mentioned by Hippocrates. It is liable to occur in epidemics, and may not appear for long intervals. Always associated with periods of famine, it is most likely to attack those suffering from hunger and destitution. It has most frequently been observed to be present during epidemics of typhus, and no doubt this fact led to considerable difficulty of diagnosis in bygone days. While it has appeared in the British Isles on several occasions during the present century—notably in 1817–19, in 1826, in 1843, in 1847–48, and in 1868—there has recently been so little that few physicians have had the opportunity of observing its course. Its prevalence in Ireland during the famine has led some writers to describe it as a disease endemic in that country, but Moore conclusively proves that this view is erroneous. Russia has had frequent epidemics, and this fever was one of the hardships which the French army had to support in their retreat from Moscow in 1812. In India, also, during periods of famine, the disease has been fairly common, but in many of the famine-stricken districts in that country there was no appearance of it in 1897. The last time the fever occurred in Edinburgh was in the year 1870, and it is to notes of this epidemic by Muirhead, by whom the cases were treated, that we are indebted for the clinical history of the disease given below.

Etiology.—*Predisposing causes.*—Most observers agree in stating that males are more frequently affected than females. It has been suggested that this is due to the fact that males preponderate in the "tramp" class, which seems so liable to the disease. As regards age, it may be said that all ages are attacked indiscriminately.

Famine, as has been mentioned above, is undoubtedly one of the most important of the predisposing causes. But while this is so, it is interesting to remark that in the last outbreak in Edinburgh, not one of the individuals attacked could be said to be underfed. The absence of destitution, therefore, does not in any way contradict the existence of the disease.

Overcrowding must obviously favour the propagation of any contagious disease, and it is usual to find that the majority of patients suffering from this fever have been living crowded together and with very insufficient air space.

Exciting cause.—Obermeier, in 1873, discovered in the blood of relapsing fever patients the organism which bears his name—the *Spirochæta Obermeieri.* This is a spirillum, and consists of a delicate spiral filament with a length of from two to six times the diameter of a red blood corpuscle. From experiments on monkeys, it has been established that the spirochæte is really the cause of the disease. It is found in the blood in vast numbers, many specimens being seen in a microscopic field. It is

freely motile, and moves rapidly with a twisting motion across the field, displacing the blood corpuscles as it goes. Even under a low power this movement of the corpuscles may be noticed, and may suggest to the trained observer the presence of the organism.

The spirillum stains well with Löffler's methylene-blue. It has not yet been cultivated successfully on any artificial medium, the experiments on animals having been made with the blood of patients. It lives, however, outside the body, and may be kept for a considerable period in sealed tubes. It is readily killed by heat, a comparatively low temperature being quite sufficient to destroy it.

During the course of the disease the spirillum is found in the blood till the time of the crisis. The numbers diminish slightly just before the crisis, and the organism cannot be found when the temperature has reached the normal. During the apyrexial period it is absent, but returns again with the second attack of the fever. It has been discovered that, on its original disappearance, it is taken up by the spleen, where it is destroyed by the leucocytes. Monkeys, deprived of their spleen and inoculated, died, and the spirillum was found after death in the general circulation.

Mode of infection.—Direct contact with a person suffering from the disease seems to be the most common method of spreading it. Entering a badly ventilated room occupied by a patient, is quite sufficient to cause the fever. It would seem, therefore, that, as in typhus, the poison may be conveyed through the air, but free ventilation renders its spread very improbable. The great incidence of the disease among hospital laundry-women makes it probable that fomites can convey the infection.

Morbid anatomy.—In the few fatal cases which have been recorded, no characteristic anatomical changes were seen, and the post-mortem conditions are only those resulting from pyrexia.

Symptoms and course.—*Incubation.*—This is very variable. Occasionally a few hours only elapse from the moment of infection to the appearance of the fever. On the other hand, fourteen days seems to be the maximum period. On an average, from five to ten days appears the most likely time.

The *onset* of relapsing fever is invariably sudden. The patient, while at his ordinary occupation, may be seized with intense headache, giddiness, chilliness or rigors, and vomiting. The headache is usually frontal, and pains in the limbs and back are common. The preliminary chilliness, or so-called cold stage, is succeeded quickly (within a few hours) by a feeling of burning heat, and the temperature is found to be considerably elevated—104° to 108°. The pulse rate runs up at the same time.

The feeling of giddiness, which appears to be a characteristic symptom of the fever, makes the patient take to his bed at once. Occasionally, even at this early period delirium may set in, but as a rule this symptom is deferred for some days. The tongue is usually thickly coated with white or yellowish fur, and in most cases remains moist throughout the illness. Diarrhœa at this stage is rare, the bowels rather inclining towards constipation. The urine is high coloured, and is not appreciably diminished in amount. The skin is usually very dry, though slight sweats sometimes occur in the first twenty-four hours. A slight icteric tinge of the conjunctivæ is usual, and in some instances jaundice is very marked. The liver and spleen are both enlarged, and are tender on palpation.

The high fever persists from about five to seven days, the temperature varying from 102° to 108° in different cases. The morning

temperature is usually lower than that in the evening, though on the third day the evening temperature seems to have a tendency to be lower, being often at the same level, and rarely higher than that of the morning. The pulse is in most cases over 110, quite commonly over 120, and in bad cases may reach a higher level. During the course of the fever the patient is very restless and often exceedingly prostrate. Thirst is intense, and is always present. Vomiting is a frequent symptom, and after the contents of the stomach have been evacuated there is great retching of bilious material and occasionally of blood. In bad cases the patient may become congested or livid about the face.

At a period varying from the fifth to the seventh day, the crisis is ushered in by slight diarrhœa, by a temporary increase in the temperature, and occasionally by delirium. The fall of the temperature is very remarkable, the sharpness of the crisis being probably unparalleled in any other disease. A fall of 10° F. in twenty-four hours is apparently common, and even this figure has been exceeded. The temperature
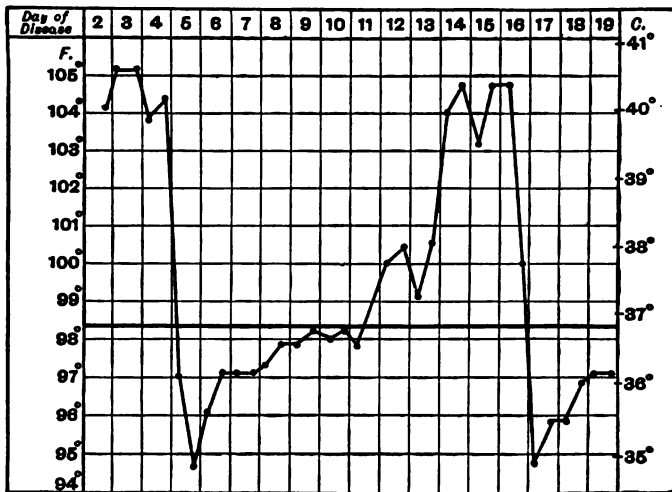
Fig. 5.—A case of relapsing fever.—After Muirhead.

usually falls far below normal, and in one of Muirhead's cases registered 92°—a somewhat alarming level. Coincident with this fall of temperature is a very profuse perspiration, and as a consequence the urine at this period is greatly diminished in amount.

After this brief period of pyrexia, which may be described as the *first paroxysm*, the patient enters the *first period of apyrexia*. His temperature, remaining at first subnormal, gradually resumes the normal level. His tongue is clean, his appetite is good. He has quite lost the feelings of giddiness and of prostration which originally compelled him to take to his bed, and about four or five days after the crisis it may be difficult to dissuade him from walking home from the hospital, a feat which he is perfectly capable physically of performing. But about fourteen days after the time he was originally taken ill, and from seven to nine days after the crisis, he is suddenly seized again with similar symptoms, and enters the stage of the *first relapse.*

The *first relapse* has rarely any premonitory symptoms. Occasionally a slight feeling of malaise may precede it, but the temperature usually

rises suddenly, at least 3° F., and the patient suffers from shivering or rigors, as in the first paroxysm. The symptoms are merely a repetition of the original attack. Occasionally the relapse is more severe; usually it is milder, or of equal severity. Vomiting, jaundice, diarrhœa, may all be troublesome. The usual point of difference is that the relapse seldom lasts so long as the first paroxysm. It varies in duration from three to five days as an average, although longer and shorter periods have been recorded.

During the first paroxysm the urine voided is in amount about the same as in health, but during the relapse its amount is considerably increased. This increase is to be particularly remarked just before the crisis, when some of Muirhead's cases passed 6 or 7 oz. every hour, and one case passed 84 oz. in the day.

The *second crisis* is in every way comparable to the first. The temperature usually reaches its acme just before its occurrence, and then falls suddenly and with great rapidity to some degrees below normal. Sweating, which has been already said to be a feature of the first crisis, is still more markedly a concomitant of the second, and sudaminal rashes are frequent at this period. Prostration is also a well-marked symptom, as is only to be expected after such a depression of temperature. The amount of urine is now naturally decreased.

The patient now enters the *second period of apyrexia*, which may in most cases be said to be coincident with *the stage of convalescence*. But in some patients *a second relapse* may occur, appearing usually about the twenty-first day from the commencement of the first paroxysm. This rarely lasts more than three days, and is ordinarily of a milder character than the previous attacks. In rare instances third and fourth relapses have been reported.

Convalescence is not so rapid as in typhus, and indeed may be said to be protracted and apt to be interfered with by the occurrence of various sequelæ.

Analysis of symptoms and complications.—*Alimentary System.*— The tongue is always coated, the fur being yellowish or grey. It is, however, usually moist. In severe cases it may become dry or brown. Thirst is constant. Vomiting is nearly always present, and may be dangerous. Nausea, without vomiting, may occur. The appetite is lost in the first paroxysm, but is particularly good in the first apyrexial period, and may last through the first relapse. The bowels are, as a rule, confined, though diarrhœa may precede the crisis.

The chief complications referable to this system are pharyngitis, dangerous vomiting, severe diarrhœa, or dysentery.

Circulatory and Hæmopoietic System. — The pulse is increased in rapidity, varying as a rule from 110 to 130 beats per minute, and rising and falling with the variations of temperature. It may become excessively rare after the crisis. In bad cases it may reach 160 or more. It is usually full during the paroxysms, and may become very dicrotic during the periods of apyrexia. The first sound of the heart is weakened.

The spleen is invariably enlarged, and this enlargement may persist into convalescence. As a rule, however, its size is decreased during the apyrexial period, and the organ becomes enlarged again with the onset of the relapse.

In old and feeble patients the complication to be dreaded is heart failure, to which cause most of the deaths are due.

Respiratory System.—Bronchitis is not uncommon, and occasionally

pneumonia may complicate the fever. Œdema glottidis and laryngitis are also met with.

Genito-urinary System. — The variations in the quantity of urine passed have been alluded to above. Albumin is present in small amount in about one-fourth of the cases. Chlorides are diminished.

Abortion of pregnant women is almost invariable, and usually occurs during the relapse.

Nervous System. — Headache is very common, and may be very severe. Giddiness is practically constant. All patients are restless and uneasy. Insomnia is also common, and is sometimes due to intense neuralgic pains, usually limited to the larger nerves. Delirium may last throughout the fever, but is generally not seen till just before the crisis, and it often is absent altogether.

Integumentary System.—The skin is always yellow, and jaundice may in some cases be very well marked. Just before the crisis the face is apt to become congested and purple. The skin is pungently hot and very dry, and is said to have a characteristic and unpleasant odour. Eruptions, resembling that of enteric fever, are occasionally but rarely met with. Petechiæ and small hæmorrhages into the skin are sometimes observed. In connection with this, we may mention that epistaxis is not an uncommon complication. The profuse sweatings and sudaminal rashes occurring at the periods of crisis have been already alluded to.

Sequelæ.—The most important of these is ophthalmia, which seems very liable to supervene in convalescence. Glandular enlargements in the groin, neck, and parotid also occur. Œdema of the lower limbs is not infrequently noticed, and amongst other sequelæ may be mentioned slight paralysis and otorrhœa.

Diagnosis.—The detection of the spirillum under the microscope is the best and surest method of diagnosis, but in default of this it will depend chiefly on the existence of an epidemic, on a sudden onset of high fever, with giddiness, slight jaundice, and vomiting, and on the marked crisis, with subnormal temperature about the seventh day. The conditions with which the fever is likely to be confused are influenza, typhus, and malaria. The occurrence of the relapse will probably clear up any difficulty.

Prognosis is always good except in old persons or complicated cases. The death rate is usually below 6 per cent. Severe diarrhœa, extreme jaundice, and excessive prostration are the symptoms which will give reason for most alarm.

Treatment.—There is no specific treatment for the disease. It is advisable to merely support the patient's strength and treat complica·tions as they arise. A tonic treatment of strychnine or nux vomica seems to give good results. Sleeplessness may have to be combated, as may also vomiting and diarrhœa. If the temperature is over 106° F., cold packing may be resorted to.

Many drugs have been tried to prevent the occurrence of the relapse. Quinine appears to exercise no favourable action. Experiments with sero-therapy have been made in Russia, but in the meantime their success is doubtful, and we must be content to adopt an expectant treatment and see that the patient is properly nursed.

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TYPHOID FEVER.

Syn., Enteric Fever; Bilious Remittent Fever; Infantile Remittent Fever; Pythogenic Fever. Fr., *Dothién-entérie; Fièvre typhoïde; Fièvre gastrique;* Ger., *Abdominaltyphus.*

An infectious fever of about four weeks' duration, characterised by a peculiar course of the temperature, especially in its early stage; by a lesion of the bowels, accompanied in general with abdominal tenderness and diarrhœa; by the appearance of a rose-coloured eruption on the skin; and by great prostration of strength.

History.—The full identification of this fever belongs to the nineteenth century. Prior to this, symptoms corresponding to those of typhoid fever had been described, and even the intestinal lesions noticed by many writers, especially by Spigelius, Panardius, Willis, Sydenham, Baglivi, and Hoffmann, in the seventeenth century; and by Lancisi, Manningham, Huxham, Morgagni, Andral, and many others in the eighteenth century; but it is clear no sharp distinction was drawn between cases presenting these characters and others of the fevers which prevailed more or less in these times.

A most important advance towards a knowledge of this disease was made when, in 1818, Bretonneau of Tours recognised the connection between certain febrile symptoms and the existence of lesions in the solitary and agminate glands in the ileum. Regarding these as of inflammatory character, he named the disease *dothién-entérite* or *dothién-entérie.* Louis, in 1829, published his celebrated work on this malady, which gave the most complete account of it that had hitherto appeared, and he it was who first gave it the name of *fièvre typhoïde.*

Notwithstanding these observations, there still existed much confusion and uncertainty respecting the relation of this to other fevers, especially to typhus. Thus in France, where the subject of typhoid fever was most thoroughly investigated, and where indeed the disease appears to have widely prevailed during many years, there would seem to have been no attempt made to discriminate between this and others of the continued fevers. In England, again, where, notwithstanding cases and even epidemics of what in all likelihood was typhoid fever had been from time to time recorded, such seem to have been regarded merely as forms of typhus, which was the infectious fever most generally met with and described. A nearer approximation to a precise distinction between those fevers was made in Germany, where they were recognised as *typhus exanthematicus* and *typhus abdominalis* respectively.

The advance of clinical study led to more minute observation of the symptoms and pathological changes attending these fevers, and their non-identity came to form a subject for discussion among physicians. Gerhard and Pennock of Philadelphia in 1837, Shattock of Boston in 1839, and A. P. Stewart of Glasgow in 1840, all made contributions of the highest value towards making clear the distinctions between typhus and typhoid fevers, both from the clinical and pathological standpoint; and the matter was finally set at rest by the celebrated papers of Sir William Jenner, published between 1849 and 1852.

Etiology.—The etiological conditions associated with typhoid fever embrace age, sex, climate, season, but especially infection and the specific micro-organism of the disease, its mode of propagation, and the various ways of its introduction into the human body.

Predisposing causes.—*Age.*—Typhoid fever is a disease of early life. The majority of cases occur between the ages of 10 and 25. It is frequently enough seen before 10, but it is not recognised as a disease of infancy, although cases are recorded of its occurrence at 6 months, and even in the new-born. It is exceptional after 40 and very rare after 60.

Sex.—There seems almost no difference between the liability of the two sexes to typhoid fever, but probably a slightly greater proportion of males are affected.

Climate.—Typhoid fever is met with in all parts of the world, and while at one time it was regarded as more liable to occur in temperate climates, it is now recognised as a very common fever of tropical countries, although its identification is liable to be more difficult by reason of its resemblance to other febrile disorders. It may be regarded as endemic in most countries, with a liability to local epidemic outbreaks, to which unfavourable sanitary conditions largely contribute.

Season.—Autumn is the season in which typhoid fever specially prevails, the rains of this time of year doubtless favouring the passage of the poison into sources of drinking water. Hence it has been called autumnal or "fall" fever.

Infection.—Long after the distinctive characters of typhoid fever had been clearly established, the nature of the disease poison and the conditions of its propagation continued to be a subject of inquiry, and numerous views were held among authorities. Of these only two need be here referred to—

The view of Murchison, who held that typhoid, like some other fevers, might originate *de novo*, if certain conditions deemed favourable for its development were present. The existence of decomposing organic matter and its access to drinking water, to air, etc., were regarded as a sufficient cause for an outbreak of typhoid in the individual or in a community, without the necessary presence of a previous case. Holding this view, Murchison named the disease pythogenic fever (πύθομαι, I decay).

The view of Budd, who held that the fever was specific in its nature, and could arise only from a pre-existing case. This latter view was that which gained widest acceptance, and the vehicle of the conveyance of the disease was recognised as being the intestinal discharges.

The progress of sanitary science, and the bearing of the germ theory upon the nature and spread of infections, gave a special direction to the inquiries into the causes of typhoid fever, and the result has been the discovery of the specific infecting agent in this disease.

Bacteriology.—Eberth, in 1880, succeeded in finding small masses of bacilli in the Peyer's patches, mesenteric glands, spleen, and other organs of a series of cases which had died of typhoid fever. His claim that these bacilli were the cause of the disease was supported by the experiments of Gaffky, who investigated their life history, and succeeded in cultivating them on various media. Other observers have caused death in small animals by the injection of pure cultures of this bacillus, and quite recently Remlinger has succeeded in producing a disease, apparently identical with the fever as it occurs in man, by feeding rabbits on lettuce watered with water containing the bacillus. Klein, moreover, has found this bacillus in drinking water during epidemics, and at present the evidence is distinctly in favour of its really being the cause of the disease.

The bacillus of Eberth (*Bacillus typhosus*) is a short thick rod with rounded extremities. In young cultures, however, elongated filamentous

forms are frequently seen. It is actively motile, as may be readily demonstrated by the examination of "hanging-drop" preparations. It is provided with numerous flagella, but the detection of these requires special methods of staining. The bacillus itself stains well with carbolic, methylene-blue or gentian-violet.

The chief difficulty with which we have to contend when endeavouring to isolate the bacillus, either from suspected water or from the organs of an enteric patient, is the great resemblance which it bears to the *B. coli communis.* The fact that this latter micro-organism is normally present in the intestine, and rapidly multiplies when any intestinal disease exists, makes it impossible to differentiate the two germs in the stools by direct examination, and it is necessary to make use of cultures on various media in order to arrive at any definite conclusion. Eberth's bacillus gives a colourless growth on potato, it does not liquefy gelatin, and it neither forms indol in the course of its growth, nor curdles milk. The *B. coli communis,* on the other hand, gives a brownish scum on potato, and, as regards the other points mentioned, produces an exactly opposite effect. Recently the Widal reaction (to be alluded to later) has been used to distinguish the two bacilli, and although it does not appear to be absolutely reliable, it cannot fail to be of great service in making this differentiation.

To demonstrate the bacillus in the tissues, it is necessary to stain sections of the spleen, liver, or mesenteric glands. If a case terminates fatally in the early days of the disease, the bacilli may also be seen in the congested Peyer's patches, but once necrosis has set in they are not so readily detected. It need hardly be said that cultures must also be made, as the *B. coli communis* has been found in all the situations mentioned. To obtain cultures the spleen is usually the organ selected, as Eberth's bacillus abounds there in well-marked cases, whereas the *B. coli communis* is not likely to be present in such large numbers. The reverse is the case with the stools, from which it is very difficult to get pure cultures of the typhoid bacillus except during the first week of the fever.

Cultures of the pure bacillus may be made on agar, gelatin, or bouillon. They grow quite well at the temperature of the room, but if a young and active culture is desired they should be incubated at 37° C. A streak culture on agar shows a bluish-grey film of growth with no special characteristics. The bouillon culture shows a uniform turbidity.

The *B. coli communis* appears to play a secondary part in the production of the disease. It has recently been noted by various observers, that not only is this bacillus more virulent when obtained from a case of typhoid fever, but that the virulence of Eberth's bacillus is increased in the presence of the coli bacillus. The same may also be said of a third bacillus, which has marked resemblances to the two mentioned above, the *B. enteritidis* of Gärtner. We must await further experiments before the exact rôle of these three organisms in the causation of the various symptoms of typhoid fever is finally determined.

Vehicles by which the bacillus is transmitted.— *Water.*—The fact that the poison of typhoid fever is in most cases carried by water has been long recognised, and instances of epidemics depending on a faulty water supply are only too common. Recently the detection of the specific bacillus in suspected water has completed the chain of evidence, but, considering the great difficulties of analysis, it would be at present premature to accept a water as safe, merely because the presence of the typhoid germ cannot be proved.

The following are fair examples of epidemics, depending on contaminated water:—

In the winter of 1896–97 an outbreak occurred in the small town of Halstead, in the county of Essex, and was reported by Thresh. On 17th November 1896, a man suffering from typhoid fever was admitted to an isolation hospital, standing on a hill on the outskirts of the town. The subsoil water of this hill supplied a drinking fountain on a public road, and the surplus water from this fountain supplied one cottage only. On 28th December a workman residing in this cottage was attacked by the fever. Shortly afterwards, four children, all of whom acknowledged drinking frequently at the fountain, developed the disease. On investigation, it was found that the hospital sewer was defective, and the water pipes passed underneath it. It appeared that after heavy rains the leaking sewage was washed into the water pipes, which were of rough construction, and so contaminated the supply of the fountain and of the infected cottage. Water collected after a rainfall was found to be turbid, and the bacillus of Eberth was successfully cultivated from it.

Maidstone has recently suffered from an epidemic, no less than 2000 persons being attacked by the disease. The water supply was undoubtedly to blame, the majority of the patients obtaining their water from the same company. The bacteriological investigations, however, have unfortunately not been very successful, and have given rise to some controversy.

Milk.—Milk, it is well known, is very readily contaminated by germs, and several epidemics in this country have been traced to such a source. The contamination may occur from infected water being used to adulterate the milk, and even to wash the milk cans, or from the cows being milked by some person who is at the same time nursing a case of typhoid fever. Such transmission is all the more likely to occur, as infected milk shows no physical change.

Harvey Littlejohn has reported an epidemic occurring in Edinburgh in 1890, when sixty-three persons, residing in different parts of the town, and supplied by seven milk-shops, were affected with typhoid fever. On investigation, it was found that all these shops were supplied with milk from one farm. The farm itself was in an exceedingly insanitary condition, its water supply being particularly bad. Moreover, one of the children of the dairyman was found to be suffering from the fever. The main interest of this outbreak lies in the fact that at first sight these cases appeared to have no connection with each other, and were scattered irregularly over a large area.

Food.—Cayley mentions a Swiss epidemic, where a large number of persons, who partook of meat from a diseased calf, developed the fever. It appears that in Switzerland cattle are occasionally affected with what seems to be a form of typhoid fever.

Recently oysters have fallen under suspicion, as being a not infrequent source of the disease. It appears that oyster-beds are occasionally placed at the mouths of rivers and near sewage effluents, and it is not difficult to conceive that contamination may occur. Several epidemics have given colour to this belief, and it appears probable that restrictions will be placed on the cultivation of oysters in certain localities. Cockles eaten raw are also suspected of having given rise to typhoid at Exeter in 1899.

Air.—Foul air, especially in the form of emanations from sewers, has been long accused of causing typhoid epidemics. Since, however, the prominent part played by water has been proved, there is reason to believe

that the risks of aërial infection have been much exaggerated. We must admit, nevertheless, that such infection occasionally occurs, and Chour has recently found the specific bacillus in the dust of a barrack-room in which the fever appeared to be endemic. The rare cases also of patients, admitted with other diseases, contracting the fever in hospitals where typhoid cases are nursed in general wards, suggest that the dust of dried stools, carried by the air, may cause the infection. This view has certainly been strengthened by a village epidemic in France, reported by Jeannot in the spring of 1898. The stools of a typhoid patient appear to have been carelessly thrown on the street, and, mingling with the dust, caused an outbreak of the fever. The water supply was found to be chemically and biologically above suspicion, and the persons chiefly affected were the children who were accustomed to play in the street. As, moreover, after the street was swept and watered no further cases occurred, there seems little doubt of the part played by the dust in the causation of this epidemic.

Fomites.—Linen and clothes soiled by typhoid patients have transmitted the disease to nurses, laundresses, and others. It is consequently very necessary to disinfect carefully all articles which may possibly have been exposed to the dejecta of the patient.

Typhoid fever is not directly contagious. Cases occurring among nurses and attendants can be attributed to a want of care in cleansing the hands, or possibly to allowing stools passed in bed to dry on the sheets and to be inhaled as dust.

Immunity.—While it is probably the fact that certain persons are less liable than others to contract typhoid fever, the only protection is a previous attack of the disease. Second attacks of the fever, though not unknown, are certainly rare. Recently it has been suggested that some persons are born immune, this view being based on the fact that a very large number of native children in India give the serum reaction to be alluded to later. It is more probable, however, that these children have passed through mild attacks of the disease in their infancy, the sanitary conditions under which they live being such as to conduce to that being the case.

Wright, starting with the principle that the serum reaction is a proof of immunity, has recently introduced vaccination for typhoid fever. By injecting dead cultures of the bacillus, a slight illness of a few days is caused, and the blood gives the reaction. But at present it is too early to say whether the persons so treated are immune.

Pathology, and morbid anatomy—The bacillus of Eberth probably obtains entrance to the body, in the vast majority of cases, by the alimentary canal. Even in those instances where there is reason to suppose that the poison has been inhaled, it is easy to see how the germs may find their way down the pharynx. Certain cases, however, which are complicated from the outset with pneumonia, probably contract the disease through the lungs.

As regards the subsequent processes, there is no little uncertainty. It has been usual to regard the disease as one primarily intestinal, with subsequent general manifestations. Sanarelli, however, regards it as primarily general, with subsequent local symptoms chiefly intestinal, and suggests that the inflammatory condition of the intestine is due to the elimination of the toxines given off by the bacillus. The bacillus itself has certainly been discovered in all parts of the body, though curiously enough it is rarely found in the blood ; and, in support of Sanarelli's views, we may cite the fact that even cases presenting in life all the classical symptoms

of the fever, have been found after death to have a perfectly normal intestine, even though pure cultures of the bacillus may be obtained from the spleen and elsewhere. Moreover, many of the severest cases show extraordinarily little intestinal disease when examined post-mortem.

Without entering further into this question, we may accept it as a fact that the bacillus of Eberth has a preference for certain organs, and it appears to select specially the Peyer's patches in the lower part of the ileum, the solitary glands in the same locality, the mesenteric glands, and the spleen. It has also been frequently found in the liver, kidneys, and lungs. In these various positions it appears, after a certain period, to set free toxines, to the action of which we may presume the general symptoms of the disease are due.

Changes in Peyer's patches.—The affection of Peyer's patches, after the bacilli have obtained a nidus within them, appears to be primarily an *infiltration* with leucocytes. The patch becomes pinkish in colour, and is gradually raised above the level of the surrounding mucous membrane of the intestine. The patches show a varying degree of hardness, some being very soft and of a dark red colour when they are fully developed, while others are paler, firmer, and more raised above the surface. French authors have distinguished these by the names of *plaques molles* and *plaques dures* respectively, but the distinction is of little importance, as the process is apparently the same in both cases.

After the process of infiltration has continued for a period, which varies in duration in different cases, the second stage, that of *necrosis*, commences. The enlarged mass gradually sloughs away, either as a whole or more frequently in detached fragments. It is probable that this change begins about the tenth or twelfth day of the fever, and that occasionally in abortive cases it is dispensed with altogether, the gland resuming the normal by a process of absorption. If necrosis does occur, the sloughing mass becomes greyish in colour, and is frequently stained a bright yellow on the surface.

The separation of the slough is usually complete by about the end of the third week, by which time the typical *typhoid ulcer* is formed. The ulcer may show a varying degree of depth, the muscular coat being frequently involved, while occasionally the base is formed by the peritoneal coat completely denuded. In shape it usually corresponds to the outline of the Peyer's patch itself, but occasionally, owing to the gland having sloughed only in part, it may assume very irregular forms. Its coalescence, moreover, with other ulcers or with diseased solitary glands may present an ulcerated surface of considerable extent and irregular outline. It may be distinguished from tuberculous disease by its long axis being parallel to that of the bowel, and its primary situation being opposite the peritoneal attachment of the gut. Its edges, moreover, do not show that induration which is so characteristic of both base and edges of the tuberculous ulcer.

The typhoid ulcer has three possibilities before it. It may become chronic and exist for several weeks before taking on a healing process, it may perforate, or, lastly, it may, and usually does, undergo a process of repair.

Perforation of the ulcer may occur in three ways. First, there may be a gradual extension in depth of the necrotic process, which ultimately reaches the peritoneal coat and works through it. In such a case, which is most usual, the perforation is usually small; hardly larger, indeed, than an ordinary pin's head. Second, the whole Peyer's patch, including the entire thickness of the tissues beneath it, may slough completely away, and as it were drop out, leaving an opening corresponding to the size of

the gland itself. Third, in certain cases where the slough has separated, and where the floor of the ulcer is formed merely by the peritoneal coat, the latter may give way and present the appearance of having been torn across.

In looking for a perforation post-mortem, great care has to be exercised in the handling of the bowel. In such cases there is always more or less peritonitis, and flakes of purulent lymph occasionally hide the lesion. Before removing the bowel, it is advisable to examine the most acutely inflamed parts *in situ*, gently wiping off any adherent lymph with a sponge. Attention will first be paid to the last foot of the ileum above the ileo-cæcal valve, the vast majority of perforations occurring in that locality. If, after removal, the bowel is flushed through under a tap, artificial perforations may readily occur. It is safer to open the gut before washing it, allowing merely a gentle stream of water to trickle over it and wash away the fæcal matter.

Repair.—If, after the separation of the slough, the ulcer escapes perforation, it gradually heals. Small granulations appear on its surface, and these are gradually covered by the mucous membrane growing in from the edges. Very little true cicatricial tissue is formed, and, as a result, there is no contraction of the gut. A few weeks after the disease has terminated, all that can be seen is the so-called "shaven-beard" appearance, minute black dots on a greyish surface. The glandular tissue, however, is not restored.

Other intestinal changes.—A process similar to that detailed above occurs in the solitary glands. Occasionally, indeed, these glands are alone affected, Peyer's patches completely escaping, thus giving rise to what has been termed the "pustular" form of the disease. In many instances the glands of the large intestine also ulcerate, particularly those in the neighbourhood of the ileo-cæcal valve. The vermiform appendix is sometimes ulcerated, and perforation may occur in this locality.

The mucous membrane of the intestine is frequently brightly injected, and the position of the ulcers may be marked on the external surface of the bowel by patches of deep congestion. The bowel wall itself in severe cases shows very marked thinning and atrophy.

The mesenteric glands are always enlarged, often to a considerable extent. They are pinkish in section, and occasionally are softened and diffluent in the centre. Cultures of Eberth's bacillus may be obtained from them, but the *B. coli communis* is often also present.

Changes in other organs.—The *spleen* is dark in colour, and almost invariably is much enlarged, being often three or four times its natural size. Occasionally it is diffluent. On microscopic examination, small masses of bacilli may be seen lying in the cells. If cultures are desired, the post-mortem examination should be made well within twenty-four hours after death, or a hypodermic needle used to suck up a little of the pulp from the organ.

The *heart* shows degeneration of the cardiac muscle, with occasionally marked thinning of the walls. It is usually pale and flabby.

The *other organs* show no special or characteristic change, though ulcerations are sometimes found in the larynx and pharynx, and the lungs of severe cases show more or less hypostatic congestion.

Symptomatology.—The period of *incubation* in typhoid fever is by no means settled. It has been stated at as long a period as three weeks and as short as one week. During this time the patient may or may not feel ill.

The *invasion* is less marked in a large proportion of cases than that of any other fever, and it is a practical difficulty to ascertain accurately the exact day of the commencement of the disease, even when the case is brought under observation early. Moreover, the patient may occasionally go about during a considerable time after the symptoms have set in.

The general clinical history of an average case of typhoid fever may be conveniently described, according to the weeks of its progress as follows:—

EVENTS OF THE FIRST WEEK.

The onset is marked by feelings of chilliness with discomfort and languor, and a sense of feverishness, more especially at night. Headache is an early symptom. It may assume the form of severe neuralgic pain, and may be located in one side of the head, or, on the other hand, there may be only the dull frontal headache, so often accompanying feverish attacks. Giddiness is often complained of, particularly on sitting up. Epistaxis, slight or severe, is not uncommon at a very early stage, and indeed the occurrence of this symptom, especially when accompanied by febrile pheno-
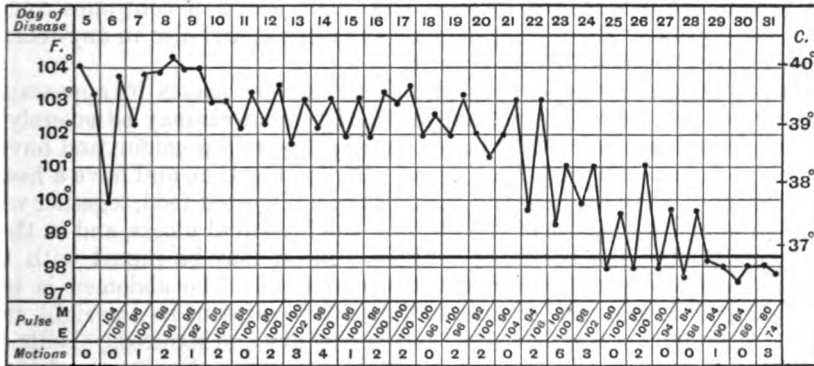
FIG. 6.—A moderately severe case of typhoid fever in a female, æt. 22.

mena, may well arouse a suspicion of typhoid. There is thirst, loss of appetite, and occasionally gastric irritation with sickness. The tongue is moist, with a somewhat creamy fur on the dorsum, and redness of the tip and edges.

The temperature is one of the most noteworthy and characteristic symptoms of this period. It shows an evening rise of 1° or 2°, a fall of 1° or less next morning, succeeded by a further rise each evening to a higher point than the preceding, along with a slight morning remission, so that the febrile movement has a somewhat climbing or step-like arrangement.

By the end of the first week, the evening temperature may have attained to the height of 102°, 103°, or more. The pulse, although quickened, is not increased in proportion to the temperature. It is full and soft. The skin is dry. Constipation is, as a rule, present. The abdomen is somewhat fuller than normal, and there may be tenderness on pressure over the right iliac fossa, where also slight gurgling may be made out. The splenic dulness is increased. By the end of the first week the patient has acquired a somewhat prostrate appearance, and the face shows a slight flush over the malar regions, especially in the evening. The eye looks lustrous and the pupils are dilated.

Events of the Second Week.

Most of the phenomena characterising the first week are intensified, and the patient appears to be more in the grasp of the disease. The temperature has risen to 103°–104°, and, while it shows slight remission in the morning, is more continuously high than during the first week. The pulse, too, is somewhat more rapid, although in mild cases it may still be comparatively slow. It is of low tension, and often shows marked dicrotism. Two important diagnostic phenomena make their appearance during this week, namely, eruption on the skin and diarrhœa. About the seventh or eighth day, on examining the front of the trunk of the body, the characteristic eruption will in most cases be observed. It consists of isolated spots from one to three lines in diameter, of rose-pink colour, slightly elevated above the level of the skin. They are most readily seen on the abdomen. There may be only a few to be noticed at first, but they increase in number, coming out in crops from day to day— the earlier spots tending to become darker red prior to their fading away. The eruption is absent in a considerable number of cases, especially in children. Other appearances of the skin are occasionally observed, especially pale bluish patches (*taches bleuâtres*). The eruption continues during the greater part of the febrile stage of the disease, and also in any recrudescences or relapses which may occur.

It is during the second week also that diarrhœa makes its appearance. Unattended as a rule by pain, the action of the bowels may be severely or only slightly disturbed. The stools are of ochre-yellow colour, and have a resemblance to pea-soup. They are of alkaline reaction, and have a heavy fœtid odour. They may contain particles of undigested food, together with epithelium and fragments of slough from the intestinal ulcers, and in them may be detected the bacilli of typhoid. Blood may be mixed with the stools: occasionally there is copious hæmorrhage. The abdomen is now more distended, and tenderness continues to be present in the right iliac fossa. The tongue is still coated, but is now dry and fissured. Delirium of mild character may be present, especially at night. During the day the mental condition is tolerably clear, but the patient is dull and listless, due probably in some measure to deafness, which is common at this stage.

Events of the Third Week.

The symptoms of the second week continue during the third, and usually in an aggravated form. The temperature remains almost constantly high, with slight morning remissions. The pulse is hurried, 110 to 120, and feebler. Diarrhœa may become more urgent. The most obvious appearance is that of greatly increased prostration. The patient lies low in bed, and has a look of apathy and weakness. He is much thinner, and his muscles are tremulous on effort. There is considerable somnolence, with low muttering delirium. Not infrequently there is cough with quickened respiration, the result of pulmonary congestion. It is during this week that the more serious complications of the fever, namely, hæmorrhage and perforation, are most apt to occur.

Events of the Fourth Week.

As a rule the fever begins to show signs of yielding—the temperature tending to fall to a lower point in the morning, while it does not attain to

such a high degree in the evening, thus tending to assume an intermittent character. A favourable change takes place in all the other symptoms, and although reduced to a condition of great weakness, the patient begins to advance to convalescence. Even during this period, however, there may arise recrudescence of the febrile symptoms for short periods, and occasionally a distinct relapse.

Some cases pass through the fourth week without any change, and there may be no signs of cessation of the fever until the fifth or sixth week. In such instances the patient becomes extremely emaciated and exhausted.

Analysis of the chief symptoms of the fever, including its more important complications.—*Invasion.*—There are few diseases where the mode of onset is so varied. On the one hand, there are cases so benign that the actual beginning of the fever escapes notice, while, on the other, the symptoms may be extremely severe; or, again, they may be mixed up with other morbid phenomena not belonging to the fever, in such a way as to render an early diagnosis a matter of difficulty.
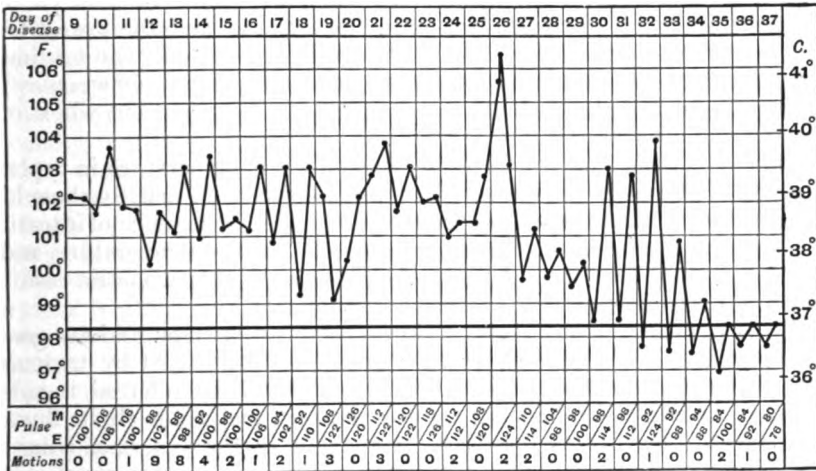
FIG. 7.—A severe case of typhoid fever, showing a tendency to hyperpyrexia on the twenty-sixth day. A male, æt. 23.

Thus pulmonary symptoms, in the form of catarrh or even pneumonia, may be the most prominent features present at the commencement of the fever; or, again, severe gastro-intestinal irritation. In the case of children, nervous symptoms, suggestive of meningitis, are not at all uncommon, and may readily mask the real nature of the disease at its onset. The so-called "ambulatory form" of typhoid includes those cases where the patient goes about for some time with the symptoms of the fever upon him, before placing himself under medical treatment, as well as those where the disease remains wholly undiscovered and untreated, until some serious complication arises, such as hæmorrhage or perforation.

Temperature.—The course of the temperature is one of the most significant features of typhoid fever. In its typical form it presents a movement which may be divided into three stages, comprehending a period of ascent, a period of continuance, and a period of decline, which in a general way might be graphically represented by the figure of a semicircle. Daily remissions in the morning, to a greater or less degree, characterise the temperature throughout.

During the first week there is a daily progressive ascent of the evening temperature, with slight morning remission, and by the end of the week in an average case the maximum is attained. During the second week the temperature is more continuously high, only such a slight remission occurring in the morning as is analogous to that of health ; and this is the case throughout the greater part of the third week, by the end of which time, however, a change in the temperature curve may be observed, the morning remissions especially being more decided and the evening rises not so great.

In the fourth week the temperature approximates to the intermittent type, that of the morning being frequently normal, with sharp rises of short duration in the evening, which, however, soon subside, and there is a steady return by *lysis* to the normal. It is generally held that the attack has come to an end when the temperature, both morning and evening, is at the normal point for at least a week, but recrudescences or relapses of the fever are not uncommon.

In observing the course of the temperature from day to day, during the progress of the fever, it will generally be found that the highest point is attained from eight to twelve o'clock in the evening, and the lowest from six to eight in the morning. As a general rule, there is only one maximum in the day, but observations taken at frequent intervals may show somewhat greater fluctuations in the temperature than can be made out when only morning and evening records are made.

Many conditions may modify the course of the temperature in typhoid. Those cases in which diarrhœa is a prominent symptom usually show high temperatures, often without much remission. The occurrence of intestinal hæmorrhage produces a sudden and marked fall in the temperature, and it has been noticed that in such cases the subsequent thermometric readings lose their typical character and become irregular.

Hyperpyretic rises (106° and upwards) are not common, and are generally of evil omen. The temperature is readily influenced by treatment with antipyretics, such as the cold bath, which will be referred to subsequently. During convalescence the temperature may show slight fluctuations from the normal, as the result of changes in the diet, or moving out of bed, and observations should be frequently taken in this stage. It is probable that the temperature in typhoid fever stands in some relation to the bowel lesion, those cases where extensive and long-lasting ulceration exist exhibiting a high and long-continuing febrile range, while relapses or recrudescences probably are associated with fresh formation or the non-healing of ulcers. Doubtless, however, short outbursts of high temperature in the convalescence may be due to less serious causes, as seen in other acute diseases. Inverse temperatures (highest in the morning and lowest in the evening) are sometimes met with, and have been occasionally observed among night nurses in hospitals when suffering from the disease. Cases of typhoid fever without febrile temperature have occasionally been met with.

Circulation.—The pulse exhibits many features of interest. In a large number of cases of moderate severity, it is in the early stage comparatively infrequent, showing a want of relation to the height of the temperature ; and in some instances this absence of correspondence continues throughout. Generally, however, the pulse tends to increase in frequency as the disease advances, and all the more if diarrhœa is present. It is at first full and soft, but soon becomes smaller and dicrotic. In the later stages of the fever, it may become unsteady and irregular. A pulse of over 120 in an adult is to be viewed with anxiety.

When hæmorrhage occurs the pulse rate increases, while the temperature falls; and, should perforation take place, symptoms indicating collapse make themselves manifest in the circulation. In convalescence, the pulse, like the temperature, should be carefully observed. Sometimes it continues frequent from sheer weakness, or from nervous perturbation. Less frequently it is abnormally rare. The heart gives evidence of feebleness as the fever advances in the weakened impulse and diminished strength of the first sound, as well as in the accompanying pulmonary congestion.

Thrombosis affecting the femoral vein—usually the left—is an occasional accompaniment or sequel of typhoid fever. It gives rise to enlargement and œdema of the limb, "swelled leg." It occurs in the later part of the fever, or in the early stages of convalescence. Although a troublesome symptom, it is rarely attended with serious results; nevertheless it is not entirely without the risk of the dangers accompanying an extension of the thrombus or its detachment. Arterial obstruction of a limb, with resulting gangrene, has been described in this as in other acute febrile diseases, but it is very rare.

The condition of the blood in typhoid fever has been investigated, especially by Osler and Thayer. It would appear that, while in the early stages of the fever little or no change is observed in the blood, as the disease advances a marked diminution in the red corpuscles and especially in the hæmoglobin takes place. There is no leucocytosis, but certain variations from the normal in the relative proportions of the different forms of the leucocytes have been detected, the polynuclear neutrophiles being diminished and the large mononuclear and transitional varieties increased.

Respiratory System.—As is the case in most febrile disorders, the respiration is quickened, and this may become very marked as the disease advances. Certain respiratory affections are apt to occur. Bronchial catarrh is a very common symptom, and is manifested by cough and the presence of diffuse moist and dry sounds. Hypostatic congestion and œdema of the lungs are apt to be present in the later stages of the fever, and may form a serious complication. Lobar pneumonia may be met with at any stage, and should it occur early may mask the symptoms of the fever. Other respiratory disorders have been described as complicating typhoid, such as laryngitis, pleurisy, etc., but they are of comparatively rare occurrence.

Digestive System.—The tongue is at first large, moist, and coated with a whitish yellow fur, except at the edges and tip, where it is red. Occasionally, for some time after the commencement, the tongue shows more markedly a febrile character, becoming dry and brown in the centre, with a white stripe on either side, the edges and tip continuing red. Later on the tongue acquires a uniform dry, red, glazed, and often fissured appearance, with some incrustation of sordes upon it. The fauces show considerable irritation in the early stage of the fever, which may lead to an error in diagnosis. In the later stage the irritable condition of the throat may become a serious hindrance to swallowing. Thirst and loss of appetite are the rule, but in mild cases neither of these may be prominent symptoms. Vomiting is not common in the early stage, but when it does occur to any great extent is usually indicative of a severe case.

Diarrhœa is one of the most characteristic symptoms of typhoid fever, but it is by no means always present. It occasionally occurs from the outset, but more commonly appears in the course of the second week, and continues

till the end of the fever, returning again in any relapse. The amount varies greatly. In average cases there may be four or five loose motions in a day, but in the severer forms there may be as many as from ten to twenty. The appearance of the stools has already been described. Although the amount of the diarrhœa does not appear to bear any necessary relation to the extent of the intestinal lesion, yet this symptom even by itself may be a source of danger, and indeed is not infrequently the cause of a fatal termination. In some cases constipation is present throughout and requires special and careful treatment, as by the incautious employment of purgatives diarrhœa may be set up. Constipation is not a favourable symptom, and should be treated.

Meteorism or abdominal distension, either accompanying diarrhœa or apart from it, is sometimes a symptom which causes much discomfort. Its persistence usually marks a severe case, and it increases the risk of perforation.

Fig. 8.—Case of a female, æt. 17, terminating fatally by hæmorrhage.

Hæmorrhage may occur at any period in the course of the fever, but it is most common about the end of the second and during the third weeks. Its amount varies, but its presence is always to be regarded with anxiety, since, although not necessarily an unfavourable symptom, it may readily become so by its amount, or by the condition in which the patient is at the time of its occurrence. The mortality in those cases of typhoid which have been complicated by hæmorrhage appears to be at least twice greater than the average. The occurrence of this symptom may be suspected by a sudden fall in the temperature, a rapid feeble pulse, on percussion dulness in the left iliac region, and marked pallor of the face. Occasionally other hæmorrhages, such as epistaxis, occur at the same time as that from the intestines, and add to the gravity of the prognosis.

Perforation is the most dreaded of all the symptoms of typhoid fever, but it is happily a rare occurrence, the proportion of cases being from 2 to 3 per cent. It is more apt to happen where the intestinal symptoms—diarrhœa, hæmorrhage, and meteorism—have been conspicuous; but it occasionally occurs where there has been constipation throughout, and in some instances in the milder or ambulatory forms. It seems more common in males than in females. The period of its occurrence is as a rule late, usually in the third or fourth week, also during convalescence, or in a relapse. It may take place without any apparent immediate cause; on the other hand, it has been seen to follow some error in diet, or exertion such as vomiting, straining at stool, and moving out of bed. It is characterised by sudden intense pain in the

lower part of the abdomen, which soon becomes diffused and general, and is followed by vomiting and symptoms of collapse; these latter are often the most reliable, as they are sometimes the only, evidences of perforation having taken place. Symptoms of peritonitis supervene, and the patient seldom survives more than one or two days. In some rare instances spontaneous recovery seems to take place, and in others surgical intervention has succeeded in reaching and closing up the perforation, although in general the patient's condition is very unfavourable for an operation. Peritonitis appears occasionally to occur without perforation.

Urinary System. — The urine at the first presents the characters common to all febrile disorders, being concentrated and dark in colour. The urea is increased in amount, especially in the early stage, and more or less throughout the course of the fever, the increase being more marked when the temperature is high. The uric acid is also increased in amount, but the chlorides are diminished, and albumin may be present to a slight extent. In the convalescence the urine regains its normal character. Acute nephritis may arise as a complication of the fever.

Retention of urine is apt to occur in severe cases, and the condition of the bladder should always be carefully watched.

A character of the urine in typhoid fever is described by Ehrlich, namely, its so-called *diazo-reaction.* This is produced as follows: Two solutions are employed—a saturated solution of sulphanilic acid in a 5 per cent. solution of hydrochloric acid; a $\frac{1}{2}$ per cent. solution of sodium nitrite.

A few c.c. of the urine are placed in a test-tube, together with an equal quantity of solution 1. To this are added a few drops of solution 2. The mixture is then rendered alkaline by the addition of ammonia which is allowed to run carefully down the side of the test-tube. At the junction

Fig. 9.—Fatal termination by perforation in a female, æt. 22.

of the ammonia with the urine a brownish red ring is formed, if the reaction takes place, and if then shaken up both the fluid and the froth are of port-wine colour. This is not present in normal urine. Unfortunately, the value of the reaction as a diagnostic is lessened by the fact that it may be met with in the urine in tuberculosis and other febrile conditions. Nevertheless, it is of use as a confirmatory test, since it is present in the great majority of cases of typhoid fever.

Integumentary System.—Besides the characteristic eruption of typhoid fever, already described, other abnormal appearances of the skin may occasionally be observed. Erythematous eruptions, more or less severe, and extensive patches of urticaria, and the still more common sudaminal rashes, all may be met with, and may interfere to some extent with accurate diagnosis. Boils and skin abscesses during convalescence are not very infrequent.

Nervous System.—The headache usually present at the outset has already been alluded to.

In the milder forms, delirium may be entirely absent throughout. In ordinary cases, however, it is not unusual after the first week, and especially at night. The type is quiet and muttering; rarely, though occasionally, noisy and violent, "delirium ferox." Associated with this symptom there is frequently some amount of mental confusion, which is apt to be aggravated by the deafness so often present. In severe forms of the fever, and in the later stages, the conditions characteristic of the "typhoid state" are observed, namely, great prostration and apathy, with muttering delirium, and sometimes coma or coma vigil. Muscular rigidity, affecting especially the legs, is sometimes present in the early stage. It may involve other muscles, such as those of the neck, and give rise to retraction of the head, very like that met with in tuberculous meningitis. Muscular tremors are frequently present in the later stages of the fever, and are usually associated with great muscular weakness. Subsultus tendinum is a common late symptom.

Convulsions are of very rare occurrence. Cutaneous hyperæsthesia is occasionally met with, especially in women and children. It affects mostly the lower parts of the abdomen and the limbs. It is apt to simulate peritonitis. Cutaneous anæsthesia is very rare, and hearing is often impaired. It first shows itself by noises in the head, which are succeeded by deafness, often to an extreme degree. Sometimes only one ear is affected. Otitis media is of rare occurrence. The existence of deafness is in some instances of considerable diagnostic value. This symptom passes away after defervescence, and it is seldom that the hearing is permanently affected.

Although vision is not much affected in typhoid fever, the eyes show some points of clinical importance. The pupils are in general dilated, and the eyes have a somewhat lustrous appearance, while the conjunctivæ are, as a rule, free from injection, such as is seen in typhus.

Relapse in typhoid fever.—The term is applied to a return of the fever during the stage of convalescence. A distinction must, however, be made between the mere occurrence of short febrile recrudescences at this period, which, as already mentioned, may be associated with changes in diet and other obvious causes, and a true relapse, in which all the phenomena of the primary attack are repeated, although usually in miniature. The relapse, which seems more often to occur in the severer forms of the fever, is announced by a gradual ascent of the temperature as at first, and by the appearance of the other symptoms, such as the increased pulse rate, dry tongue, and diarrhœa. The rash also frequently returns, but it has been noticed that it is earlier in appearing than during the primary attack. The relapse is, as a rule, of shorter duration than the original fever, and milder in character. Its effects upon the patient may, however, be very serious, particularly if, as sometimes happens, more than one relapse takes place; and while in the great majority of instances the termination is favourable, death may occur from exhaustion, hæmorrhage, or perforation. The cause of such relapses appears to be a reinfection of the system from the primary attack, and the anatomical changes in the intestine reveal the presence of fresh ulcers affecting glandular tissue which had previously escaped.

Varieties of typhoid fever.—Typhoid fever presents such differences in character, as regards severity, duration, modifications resulting from age, climate, and other conditions, that it is quite possible to recognise certain clinical types or varieties. Elaborate divisions, founded largely upon the prominence of certain symptoms, have been made, but such classifications

are of little value for clinical purposes, and are confusing. Probably all the various forms in which typhoid fever is met with might be included under the following classes:—

The milder forms.—These embrace—(*a*) Cases in which the whole course of the disease from its onset is of benign character, none of the symptoms assuming any special prominence, and convalescence being established in less than four weeks. (*b*) Cases which prove abortive, in which the characteristic features of the fever are present but are of moderate intensity, and come to an abrupt termination in from one to two weeks. It is probable that the pathological changes in the intestine are limited to infiltration of the glandular structures, which terminates in resolution, and that the usual ulceration does not take place. (*c*) The latent or ambulatory form, in which the patient, while suffering from the fever, continues to go about. This type of fever is as a rule mild, but special dangers attend its non-recognition, partly from the possibility of conveying the disease, but more particularly from the fact that such cases, being untreated, the risks of serious symptoms, such as hæmorrhage or perforation suddenly arising, are great. (*d*) Under this class might also be included the occasionally occurring afebrile forms of typhoid.

The graver forms.—These include—(*a*) Cases in which all the symptoms are severe throughout—high temperature, diarrhœa, tympanites, delirium. Such cases are apt to be complicated by hæmorrhage and by relapses, and the mortality is high. (*b*) Cases in which certain classes of symptoms, not necessarily belonging to the fever, are prominent, *e.g.* pulmonary symptoms, in the form of bronchitis and pneumonia; nervous symptoms,

Fig. 10.—A mild or abortive case of typhoid fever.

such as severe headache, suggestive of meningitis; urinary symptoms, in the form of acute nephritis; gastric and biliary symptoms, such as vomiting and jaundice. Such accompaniments may not only form complications more or less serious, but they often mask for a time the true nature of the disease. (*c*) Cases of malignant type, such as occur in all fevers, in which hæmorrhage from mucous surfaces, extravasations into the tissues occur, and those in which the symptoms from the first are intensely severe, and bring about rapid prostration and death.

Typhoid fever in early and in later life.—(*a*) In children, before the age of 5, typhoid fever, although not unknown, is uncommon; but it occurs with increasing frequency between 5 and 14. Its early recognition is sometimes a matter of difficulty, in consequence of the frequent presence of head and other symptoms, which are apt to simulate tuberculous meningitis. There are certain points in which typhoid fever in the child differs from that in the adult. Its course upon the whole is milder, and although the temperature may be high, it has throughout a marked tendency to remission, which led formerly to this disease being included under the general term *infantile remittent fever*. The rose-

coloured spots are frequently absent, and even when present are apt to be few in number. The intestinal lesions are less severe, the glandular structures in the mucous membrane of the ileum being merely infiltrated and not ulcerated, at least in young children; and while diarrhœa is common enough, hæmorrhage and perforation are extremely rare. The mesenteric glands are liable to be engaged, simulating tabes mesenterica. The course of the fever is comparatively short, but relapses are frequent. The death rate, however, is low. (b) Typhoid fever late in life is occasionally met with, notwithstanding it is well known to be rare after 40. Well-marked cases have been described in persons over 60, 70, and 80. The fever tends to be of adynamic type, and although apparently mild as regards temperature, is apt to be protracted, and during its continuance exhaustion or collapse are to be feared. The death rate is high.

In *tropical countries,* typhoid fever, although differing in no material respects from the disease in temperate climates, has a more serious significance, and the mortality is greater. The conditions of the temperature of the air are apt to accentuate the depressing effects of the fever.

Sequelæ.—Not a few of the conditions already referred to, as complications occurring during the progress of a case of typhoid fever, may be met with during or after convalescence as sequelæ. The swelled leg is one illustration of this; parotitis is another. Periostitis, affecting for the most part the shafts of long bones in adolescents, is a well-recognised occasional sequel of typhoid. Although as a rule passing off soon, in some cases an abscess forms, and necrosis or caries of the bone may remain. Abscesses may occur in the viscera; even in the brain.

The health may be affected in various ways, as the result of an attack of typhoid fever. Thus, as regards the digestive system, a chronic condition of dyspepsia may long persist, probably for the most part intestinal in character, and obviously admitting of ready explanation from the lesion of the bowels. As regards the respiratory system, phthisis is an occasional though apparently not very frequent sequel of typhoid fever. The nervous sequelæ are important, and include many forms of functional disturbance, such as hysterical conditions, the so-called "typhoid spine." But even insanity may follow this fever, as it sometimes follows typhus. Happily, as in the latter, the prognosis is good. A few cases of hemiplegia, with or without aphasia, have been reported.

Diagnosis.—While in a certain number of cases of typhoid fever a diagnosis is readily arrived at, it is frequently almost impossible to come to a definite conclusion. The disease has no single pathognomonic symptom, and we must depend on the concurrence of several signs and symptoms, no one of which is invariably present in the course of the fever. Owing to the typically insidious onset, a definite diagnosis can seldom be made in the first week.

The *history* of the patient should be carefully analysed. Malaise, nausea, headache, and insomnia are frequently complained of. If, in addition to these symptoms, the patient has suffered from diarrhœa or from epistaxis, and the temperature is found on examination to be elevated, there is a strong presumption that the case is one of typhoid fever. Sore throat or bronchial catarrh are occasionally the symptoms for which the patient first seeks relief. In other instances the complaint is of loss of appetite and indigestion, and the heavily furred tongue may suggest a gastric catarrh. If such a case does not improve, under appropriate treatment, the temperature should always be taken, and it may be found that the catarrh is due to the febrile disturbance caused by the disease.

The *physiognomy* of the patient may also afford assistance. The complexion is usually clear, and a pink, hectic-looking flush may be noticed on the cheek bones. The pupils of the eyes are larger than normal, and this gives the patient the expression of languor and ennui which is nearly always present in a true case.

If the case is seen during the first few days of the illness, the curve of the *temperature* should be carefully watched. A case which shows a temperature of 104° on the first day of the disease is almost certainly not typhoid fever. On the other hand, a step-like rise of the evening temperature, with slight morning remissions for the first four or five days, is very suspicious.

The *pulse* is accelerated, but seldom in proportion to the rise of temperature. This sign is of great value in making a diagnosis. In an adult it should average from 90 to 100, and even in children it is slower than would be expected. After the first week dicrotism is almost invariably present, and the pulse is soft.

The presence of *spots* about the seventh or eighth day of a continued fever makes the diagnosis almost certain. Their absence, however, is unfortunately of no diagnostic value. They probably usually occur, but in mild cases they have frequently disappeared before the patient comes under notice.

The tumidity of the *abdomen* is of great importance. In the vast majority of cases this sign is present, though here again its absence does not preclude the existence of the disease. There is usually tenderness on gentle palpation in the right iliac fossa. Great stress has been laid on gurgling in this situation; but, apart from the fact that this sign can often be found in cases of ordinary diarrhœa, the pressure required to elicit it is hardly advisable, unless it is absolutely certain that the fever is only a week old.

Enlargement of the *spleen* is invariable. This can usually be made out quite satisfactorily by percussion, but often, especially in children, the organ can be quite readily palpated.

Ochre-coloured "pea soup" *stools* should always cause a suspicion of typhoid fever, but it must be remembered that such stools may occur in other diseases, in which a patient with high temperature has been fed on more milk than he can digest. We may here add that the occurrence of a hæmorrhage in a case with continued fever gives an almost certain diagnosis.

The *palmar-plantar* sign of Filipovitch has recently attracted considerable attention. It consists in a saffron-yellow coloration of the hard skin of the palms and soles. While it certainly is very frequently present in adult patients with hard hands and feet, we have not noticed it so often in children, and it has been noticed in other diseases, particularly in tuberculosis. It is probably, therefore, of no great value. We may here add that marked desquamation may often be seen on the feet.

Bacteriological diagnosis.—1. *Examination for the bacillus of Eberth.* —As has been already hinted, the great difficulty of isolating this bacillus places this method of diagnosis out of the reach of all but expert bacteriologists. During the first week of the fever there is a fair chance of getting a successful cultivation from the stools; but as several days are required to distinguish the organism from the *B. coli communis*, the case will in most cases have declared itself before a definite opinion can be given. Puncture of the spleen to obtain the bacillus is more likely to give

a pure cultivation at once, but even those who have introduced and used this method with success hesitate to recommend a procedure which can hardly be free from risk.

2. *Widal's serum reaction.*—Of much greater value than the above test is serum diagnosis. Introduced almost simultaneously in the summer of 1896 by Widal and Grunbaum, it has already taken a high place in the diagnosis of typhoid fever. The test depends on the behaviour of the bacillus of Eberth, when exposed to the blood of a patient suffering from the fever. In such a medium the bacilli, previously motile and evenly diffused over the microscopic field, lose this motility and agglutinate into masses or clumps. In blood from normal persons, or from patients suffering from other diseases, the bacilli remain active, and the reaction does not occur. As the successful performance of this test requires an incubator in which to make the necessary cultures, it is hardly likely to be of much use to the general practitioner. But in hospitals it can be readily managed, and public laboratories have in many instances made arrangements to test blood sent to them. The method we have found most useful in hospital practice is as follows :—

The stock cultures of the bacillus are kept on agar or gelatin at the temperature of the room. The night before a test is required, a subculture is made on agar and incubated at 37° C. The next day the culture has grown sufficiently for a platinum loopful to be scraped from it. This is stirred into a few drops of sterilised beef bouillon in a watch-glass, and it is with the emulsion of bacilli so procured that the test is performed. The thumb of the patient is carefully cleansed, and is pricked just above the nail. The blood is drawn up in an ordinary leucocytometer pipette to the mark just below the bulb. The point of the pipette is then wiped, and sterilised beef bouillon sucked up till the bulb is filled, and the instrument is then shaken. The pipette now contains 1 part of blood to 10 of bouillon. The mixture is then ejected into a U-shaped tube, previously bent for the purpose in a Bunsen flame, and the tube is placed in a centrifuge. This brings the corpuscles down into the bend of the tube, leaving clear serum above. The centrifuging process need not be very complete, as a few blood corpuscles greatly assist the ready focussing of the microscope afterwards. Two drops of this diluted serum mixed on a celled slide, with one drop of the emulsion from the watch-glass, give a mixture consisting of a somewhat indefinite number of bacilli moving in a medium consisting of 1 part of blood to 30 of sterile bouillon. The slide is then examined under an ordinary high power.

If the blood be that of a typhoid patient, the bacilli, at first actively motile, are seen gradually to lose their activity. They cease to move rapidly across the field, sometimes spin rapidly on their own axis, and begin to show a tendency to stick to each other. First merely stuck together in twos and threes, these small groups become joined to each other, till, after a period varying from a few minutes to several hours, the microscope field presents two or three large colourless masses, consisting of immotile bacilli, and a space perfectly free from moving bacilli between these clumps. In a certain proportion of cases the clumps may be joined to each other by long strings of motionless bacilli, giving a " reticulate " appearance to the reaction. The reaction should be practically complete in four hours to be regarded as final.

Another method, recommended by Delépine, of working this test, is to draw the blood from the patient into a capillary glass tube, provided with

a small bulb. The ends are sealed in a flame, and the blood can be kept an indefinite period, and can be very easily sent to a laboratory by post. In making the dilution, a loopful of the clear serum, which has separated from the clot, is placed on a coverslip, and ten or fifteen loopfuls of a fresh culture (made in bouillon) are added and mixed. The coverslip can be then inverted on an ordinary slide.

A third method, that of Wright, depends on the fact that if the mixture of serum and culture is sucked up into a slender glass tube, and the tube left standing erect in a rack, the masses of agglutinated bacilli sink to the bottom of the tube, and form a little white plug or sediment which can be easily seen by the naked eye. This "sedimentation" test is particularly useful in laboratories, where large numbers of specimens have to be examined. Tubes containing normal blood show merely an evenly diffused cloudiness.

In performing the test satisfactorily, there are several important points to attend to. First, the subculture must not be more than twenty-four hours old. Cultures of a longer date are not nearly so motile, and occasionally show masses which may readily be mistaken for true clumps. Second, it is advisable to always return to the original stock cultures when a subculture is required, as, if there is too much subcultivating, the cultures appear to become attenuated. Third, the dilution should not be less than 1 part of blood to 25 of bouillon, as occasionally healthy blood gives a reaction, if the dilution is insufficient. Fourth, either the culture should be carefully examined under the microscope, before performing the test, to see that it is active and does not contain false clumps, or, what is still better, a normal blood, and, if possible, the blood of a known typhoid patient, should always be examined together with the new specimen, so as to give a check to the results. Should these precautions be taken, there will be wonderfully few anomalous results.

As regards the *rationale* of this test, it has been suggested that there are developed in the blood of typhoid patients certain substances which have been termed agglutinins. These substances have some chemical or physical action on the protoplasm or sheath of the bacillus, and so cause the reaction. They appear to use themselves up in the process, which would account for partial reactions taking place, should the bacilli be too numerous. Whether the action implies *immunity* is a question of some doubt. It occasionally lasts many years after a patient has had the fever. It also appears in the blood of persons vaccinated by injections of dead bacilli. In the meantime we may say that its presence certainly does not prevent relapses, which should be to a certain extent an argument against it as a proof of immunity. Perhaps it is safer at present to regard it as a reaction of *infection*.

As regards the value of the test, its presence implies that a patient is either suffering from typhoid fever, or has had, at some time or other, typhoid fever. Its absence unfortunately cannot be held to prove that the disease is not typhoid, as has been proved more than once both pathologically and bacteriologically. It is occasionally disappointing in that it may not appear till later on in the fever, when all difficulty has probably disappeared; and it is quite common to fail to get it before the second week. In our experience, however, it is by far the most accurate method at our disposal for the diagnosis of typhoid fever.

Differential diagnosis.—While in making a diagnosis attention to the principles mentioned above is usually sufficient, it will be useful to

remember the characteristics of the diseases most likely to be confused with typhoid fever. Of these the following are perhaps the most important :—

Typhus fever.—On inquiring into the history, if it is found that the patient was suddenly attacked, and can point to a sudden rigor or to marked prostration from the first day of his illness, it is much more probable that we are dealing with a case of typhus. On the other hand, if there is a history of more than a fortnight's fever, the disease is more likely to be typhoid, since typhus terminates by crisis about the fourteenth day. We may tabulate the main distinctions between the diseases as follows :—

	Typhoid Fever.	Typhus Fever.
FACE . . .	Pale with hectic flush.	Congested and bloated.
EXPRESSION . .	Languid and apathetic.	Drunken.
PUPILS . . .	Dilated, or in bad cases normal.	Contracted almost invariably.
CONJUNCTIVÆ .	Clear.	Injected.
ABDOMEN . .	Tumid and tender.	Usually normal and not tender.
RASH . . .	Rose spots fading on pressure.	Petechiæ from seventh day.
PULSE . . .	Usually, even in bad cases, infrequent.	Rapid.
TERMINATION . .	By lysis.	By crisis.

In addition to these differences, we may add that diarrhœa is not common in typhus, except occasionally about the time of the crisis. The spleen is usually enlarged more or less in typhus, and therefore much stress cannot be laid on its size. The temperature, moreover, in bad cases of typhoid may show very little of the characteristic morning remission, but may continue in almost a straight line on the chart. And, lastly, a dirty flea-bitten skin in a typhoid patient may have a striking resemblance to a badly developed typhus rash.

Tuberculosis—(α) *Tuberculous meningitis.*—This is only likely to be confused with cases of typhoid fever with marked head symptoms. In such cases the temperature is usually high, probably about 104°, and the moderately slow pulse of typhoid is usually accelerated. In tuberculous meningitis the fever is as a rule moderate and more hectic in type, and the pulse may in certain cases be less frequent than normal. The pupils, moreover, instead of being equally dilated, are often unequal, and squinting is common. An ophthalmoscopic examination may discover miliary tubercles. There is no rash on the abdomen, and the tache cérébrale can be elicited. The spleen as a rule is not enlarged and the abdomen, so far from being tumid, is in most cases retracted or "scaphoid." Vomiting, rare in typhoid fever, is not unusual in tuberculous meningitis. It has further been pointed out by Jenner, that in typhoid fever the headache ceases when the delirium begins. Lastly, the family history, the presence or absence of pulmonary lesions, and the question of possibilities of infection, may all throw light on a doubtful case.

(β) Still more difficult is the diagnosis from early cases of *tuberculous*

peritonitis. The appearance of a patient suffering from this disease may closely simulate that of a typhoid case. The tumid abdomen, before glandular masses are palpable or fluid can be detected, may also be puzzling. But the presence of either of these signs will clear up the case. The temperature of typhoid fever never falls while the abdomen remains distended; that of a tuberculosis may do so.

(γ) *Acute tuberculosis* has also frequently been mistaken for typhoid fever. The onset in this disease is more gradual, and the wasting as a rule greater. If the lungs are severely affected, the microscopic examination of the sputum for bacilli may settle the point. Again, the breathing is more rapid and the face more cyanosed, and sweating is more frequent. But in some cases it may be said that a diagnosis cannot be made, and we are reduced to considering the family history, and waiting for further developments before giving a definite opinion. It is particularly in these obscure tuberculous cases that we have found the Widal reaction most useful.

Pulmonary inflammations.—Pneumonias are very often mistaken for typhoid fever. Out of 169 consecutive cases sent in to the Edinburgh City Hospital as the latter disease, no fewer than sixteen were the subjects of pneumonia only. At first sight it would seem that it needs considerable carelessness to make such an error, but the physical signs of lung inflammations, especially in children, are sometimes so obscure that the mistake is readily made.

(α) *Acute lobar pneumonia* is usually detected by the rapidity of the respiration, although occasionally its rate may be only slightly accelerated. After a day or two the case usually declares itself, as consolidation becomes more marked, but even then it is difficult to decide if the lung condition is not merely a complication of a typhoid fever. The difficulty is increased in cases where head symptoms and delirium are marked, and sometimes the occurrence of the crisis is required to make a definite diagnosis. Herpes of the lips, so common in pneumonia, is very rare in typhoid, and its existence would point to the case being one of the former disease. The pulse also of pneumonia is frequent.

(β) *Catarrhal pneumonia* in children is frequently attended with symptoms which may suggest typhoid fever. The digestion is often disturbed, and this may lead to abdominal distension and severe diarrhœa. Careful daily examination of the chest will, however, usually decide the case, but where the patches of inflammation are very small it may be some days before a diagnosis can be made.

Influenza.—It is only the gastro-intestinal form of this fever which is liable to be confused with typhoid fever. The chief points to be noted are, the comparatively sudden onset of influenza, its characteristic pains in the back, and the frequent limitation of its headache to the frontal region. The subsidence of the fever in the second week will also point to influenza. It must, however, be remembered that the two diseases may exist together.

While the diseases mentioned above are of most importance, it is well to bear in mind that typhoid fever is also simulated by certain cases of ulcerative endocarditis, gastro-enteritis, trichiniasis, relapsing fever, and appendicitis; also by the fever which attends the secondary manifestations of syphilis. On the other hand, the occurrence of an erythematous rash and sore throat, at the outset, may lead to a diagnosis of scarlatina.

Prognosis.—Every case of typhoid fever, however mild, is liable to

serious complications and sequelæ, and therefore the prognosis will always be carefully guarded. The longer a patient has been struggling against giving in to the disease and taking to his bed, the worse become his chances of recovery.

Epidemics vary considerably in severity, and much stress cannot therefore be laid on the percentage mortality of the disease, which may vary from 7 to 20 under different circumstances. Occasionally an epidemic occurs, where all the cases are marked by severe symptoms. Again, certain persons appear to be constitutionally susceptible to the fever, and the type may be more severe in certain families than it is in others. It is said, on apparently sound statistical evidence, that females have a higher death rate than males, 1 per cent. more of those attacked succumbing to the disease.

Putting aside these more general considerations, it may be broadly said that the prognosis becomes progressively more serious as age increases. Children, in the vast majority of cases, do well. In older persons, and especially in the middle-aged, the outlook is worse.

The conditions which justify a favourable prognosis are the following:— Moderate fever, not exceeding 103° F. at night, and characterised by considerable morning remission; a pulse not exceeding 100 in the adult, or 120 in the child; a moist and not heavily coated tongue; a soft and slack abdomen; and an absence of complications. If, moreover, the patient sleeps well, and can move himself freely in bed, a favourable termination may be expected with some confidence. But it must always be remembered that the mildest cases may suffer from hæmorrhage or perforation, and it is advisable not to admit that they are out of danger till the evening temperature has been ten days normal at least.

If, on the other hand, the patient is alcoholic, if he suffers from insomnia, delirium, or subsultus tendinum, and if he lies on his back unable to turn in bed, the prognosis is distinctly unfavourable. Vomiting, retention of urine, incontinence of urine or fæces, marked and persistent tympanites, and severe diarrhœa (ten to twelve motions daily), are of very grave import. Again, a pulse of over 120 in an uncomplicated adult case, should cause anxiety. If the pulse in such a case reaches 130, there is reason for alarm. As regards the temperature, a persistent level at about 104° F., or over, without marked morning remission, points to a severe case. If this temperature is maintained in the third week of the disease, and there is no sign of a lysis, it is probable that the case will run twenty-eight days at least; and if other of the unfavourable signs mentioned above are present, the prognosis becomes very grave.

While spots have no relation, as regards their number or presence, to the severity of the case, still it is unusual to see a lysis commence as long as successive crops appear. If, as has been suggested, each new crop represents a further invasion of hitherto unaffected Peyer's patches in the intestine, it is not reasonable to expect marked improvement in a bad case as long as they continue to come out.

As regards the occurrence of the ordinary complications of typhoid fever, hæmorrhage, unless it occurs in the first ten days of the fever, must always be regarded as serious, especially if the temperature has fallen considerably and declines to rise. If, however, there is no recurrence within forty-eight hours, and the temperature has regained its original level, the patient often does very well, and sometimes seems none the worse for the accident.

Perforation is practically always fatal. Certain cases of recovery, by adhesive peritonitis having limited the leakage, and of successful operative interference, have been recorded. But at present it is safer to assume there is no hope in such a case. An operation, therefore, would always be justifiable, even though the chance of success is infinitesimal.

Relapses are, as a rule, milder than the original fever, though there are exceptions to this rule. The prognosis is, on the whole, favourable. They seldom last much more than a fortnight.

Intercurrent complications make the outlook much more serious. Pneumonic complications are, in our experience, exceedingly fatal. Renal disease, interfering no doubt with the elimination of the toxines, is of grave import. Pregnancy is nearly invariably fatal to the child, and is very dangerous to the mother. Typhoid fever, complicated by the puerperal state, is also very serious.

Treatment.—Under this head will be embraced the prophylaxis, the general management of a case both during its progress and in convalescence, and the measures to be employed for dealing with special symptoms and complications.

Prophylaxis.—This subject can only be alluded to in very general terms. Since it is mainly through drinking water that the poison of typhoid fever gets access to the body, it is clear that, whether in large or small communities, the water supply should be secured against contamination by sewage, both in its source and its distribution. This is one of the prime duties of public hygiene on the part of local authorities, and the neglect of it has been followed with disastrous consequences in only too many instances. In the case of large and populous centres, sanitary arrangements are more likely to be under immediate supervision and control than in thinly peopled country districts, or in isolated houses, where the water supply is often derived from wells and streams.

One of the most efficient of all prophylactic measures is notification. Outbreaks of typhoid fever usually make themselves manifest at first as sporadic cases, or as localised epidemics, and an efficient system of notification places in the hands of public medical officers the means for tracing their origin, and effectually dealing with it.

Nor does the water supply alone demand careful attention, but all matters relating to drainage, house sanitation (including the regular cleansing of cisterns and sinks), as well as cleanliness, in a community, form equally important considerations in respect to the prevention of typhoid fever.

When a case occurs, careful inquiry has to be made as to the existence of any previous case, and although such inquiries are often enough fruitless, it has frequently happened that outbreaks have been clearly traced to their origin. Where suspicion attaches to drinking water or to milk, these should be boiled before use. Food supplies also from possible sources of contamination should be avoided.

The disinfection and disposal of the excreta from a typhoid patient is a matter of first importance. For this purpose there seems to be no better chemical agent than carbolic acid, a solution of which, of strength 1 in 40 or 1 in 20, should be added to the stools and left in contact with for them two or three hours before they are disposed of. Other disinfectants are sometimes employed, such as corrosive sublimate (1 in 500, slightly acidulated with hydrochloric acid), but the liability of most of them to act on the pipes and other plumber work prevents their general use for

dwelling-houses, although they may be of service in places where the excreta are disposed of in pits or privies.

All utensils and vessels should be washed in the disinfecting fluid after being used. Bed or body linen soiled with the stools should be soaked in carbolic acid solution, or boiled before being washed. Nurses and attendants should cleanse the patient's perineum with a weak carbolic or corrosive sublimate solution, after stools have been passed, and should be scrupulously careful in similarly cleansing their own hands, which may have become soiled with the discharges.

General management.—The general management of a patient with typhoid fever bears reference for the most part to efficient nursing and dieting. The patient should be in a large, airy, and well-ventilated room, the temperature of which should be kept at about 60° F. There should be free access of fresh air by window or door, in such a way, however, that draughts are not likely to be felt by the patient. The bed should be moderately firm, but not hard. The nurses should keep an accurate record of the patient's temperature (which should be taken every four hours, or oftener if required), the times of feeding, the quantity given, and the amount of sleep; and also note carefully any changes in the patient's symptoms and appearances occurring during the absence of the medical attendant. The mouth of the patient should be attended to, and kept clean by boric solution or other mild antiseptic, and the whole body of the patient should be sponged daily. The skin should be kept thoroughly dry, and examined particularly at those parts where pressure bears, and the patient's position changed from time to time to obviate the occurrence of bed-sores. The patient should not be moved out of bed at least after the first week, and the urinal and bed-pan should be employed. Visitors should be excluded, and the patient kept perfectly quiet. Milk is, by almost universal consent, held to be the best food in typhoid fever, and, in most instances, it is the only article of diet necessary during the progress of a case. It is usually taken readily, even by those to whom at other times it may be distasteful. Much depends upon its mode of administration. It should not be given too often, nor in too great quantity. About 4 oz., given every two and a half or three hours, will probably be found to agree well. It may be given alone, or diluted with a small amount of pure water, lime-water, or soda-water. The total quantity given in twenty-four hours should not, as a rule, exceed two and a half or three pints. It is necessary to ascertain whether the milk is agreeing with the patient by being properly digested. The stools must accordingly be examined regularly, and should portions of undigested curd be found to any extent, the use of milk may have to be suspended for a time, or it may be reduced in amount, or diluted or peptonised. Animal broths or jellies may be substituted for a time, but while they are of undoubted use as stimulants, they do not possess the nutritive value of milk. Barley-water, well strained oat-gruel, white of egg, thin custard, etc., may be usefully employed during the time the milk feeding is reduced or suspended; but care has to be taken that diarrhœa is not induced or aggravated by such changes in diet. The food should be administered both by day and night. If the patient be unconscious, he must be roused to take the food at the regular time. On the other hand, when he is in a calm sleep, it is better in most cases not to disturb him.

Some eminent authorities have advocated the use of a solid diet of meat, and have shown what seemed to be satisfactory results. But this plan has

never been extensively adopted, and the weight of opinion is altogether in favour of the practice which, recognising in typhoid fever a condition in which the whole alimentary canal suffers more or less in its nutrition, adapts the dietary of the patient to the altered digestive and assimilative functions. Water may be freely administered, but the amount at one time should be moderate, large drinks sometimes tending to aggravate the diarrhœa.

Provided the food is agreeing, no change should be made in the patient's diet during the progress of the fever; but when the temperature becomes normal, and convalescence seems to have set in, a little more substantial food may be cautiously introduced, such as meat broths thickened with rice or barley, milk puddings, boiled or steamed fish, besides tea or coffee. But in all such changes made in the diet the stools should be examined to see that the food has been digested. At the same time the temperature should be carefully noted, and, should any material rise be observed, a return to the fever diet must be made. In no disease has convalescence to be more carefully watched.

The question of alcoholic stimulants in typhoid fever has been much discussed, and different views are held and given effect to. It is certain that all cases of typhoid do not require alcohol, and that probably there is a tendency to err in the direction of its too frequent and indiscriminate use. Many cases of moderate severity and average duration never present symptoms calling for stimulation. The indications for alcohol bear reference to the effects of the fever upon the patient's strength, and the evidence derived from the circulatory and nervous symptoms. Where the heart, as a result of long-continued high temperature or diarrhœa, shows signs of feebleness, in a weakened first sound or irregular action, and a small pulse, along with evidences of pulmonary congestion, alcohol may prove of signal service; so also when symptoms of collapse threaten. Alcohol is sometimes highly efficacious in procuring sleep, and in quelling the restlessness and delirium which often characterise the later phases of a severe attack of typhoid. The form best suited for administration is pure spirit (brandy or whisky), and, as regards quantity, no general rule should be laid down; but much must be left to the physician's judgment of the requirements of the case. It is seldom that more than 6 or 8 oz. in twenty-four hours are demanded, and care should be taken to see that it fulfils its purpose, since it may happen that alcohol may be found to increase the patient's restlessness, and thus require to be lessened in amount or discontinued. Other cardiac stimulants and tonics may sometimes be found of service, along with or in place of alcohol, such as ammonia, digitalis, and strychnine.

Diarrhœa, if slight, may require no special treatment, but in many instances this symptom assumes such proportions as to call for remedies to restrain it. Occasionally some change in the feeding may suffice to effect this, such as boiling the milk and adding lime-water or a little isinglass to it, or, as before mentioned, by suspending milk altogether for a short time, if there is reason to believe that the diarrhœa is aggravated by undigested curd. Enemata of starch, with or without laudanum, are sometimes efficacious. Opium or Dover's powder, in combination with bismuth, is one of the most soothing astringents. A mixture containing acetate of lead and morphine, the lead suppository, the mineral acids, tannic acid, pernitrate of iron, etc., may often be found of use. In the case of children, simple starch enemata, chalk mixture, or the aromatic powder

of chalk with opium, are among the safest remedies. Meteorism may occasionally be relieved by the rectal tube, or by the administration of charcoal, salol, or salicylate of bismuth. Turpentine in doses of 20 minims has been employed with success, and its external application in the form of a stupe is useful. A light application of ice over the abdomen is sometimes followed with marked benefit.

Constipation, which may exist throughout the whole duration of a case, is best treated by a small dose—a teaspoonful or less—of castor-oil, or by an enema every three or four days. The former is probably the better method. Saline purgatives, as recommended by some, are not free from risk.

Abdominal pain, which is occasionally a troublesome symptom, and may sometimes, though not always, be due to a localised peritonitis, is relieved by warm opium fomentations, or by a light ice-bag, and by opium or Dover's powder internally.

Hæmorrhage is best treated by keeping the patient entirely at rest. Morphine is the most useful drug to effect this, and may be given in the dose of 25 or 30 minims of the liquor, followed by 10-minim doses every two or four hours as required. The feeding must be reduced to the lowest possible limit, a little milk being given occasionally in quantities not exceeding a tablespoonful at a time. Of styptic remedies, acetate of lead (2½ grs. every four hours), or turpentine (20 minims every two hours), are probably the most satisfactory. If there is no further motion, the bowels can be left alone for three or four days, when an olive-oil enema may be given.

Perforation has unfortunately no real medical treatment. The pain and distress of the patient may be alleviated by morphine, but a recovery is almost unknown. If surgical interference is undertaken, it should be within twelve hours of the occurrence of the perforation, if it is to have much chance of success.

Bed-sores can be to a large extent prevented by a careful attention to the skin, and by shifting the patient's position, or by a water-cushion or bed. Where the surface is tender, it should be bathed with spirit or a lead lotion. When a sore forms, a dressing of boric or zinc ointment is useful.

The numerous complications and sequelæ of typhoid fever must be treated according to the general principles applicable to their nature.

During the whole of convalescence, and even for a long time after apparent recovery, care should be exercised, particularly as regards diet, over-fatigue, etc. In this way not only may immediate risks be prevented, but a condition of long-continued weak health and dyspepsia, from which many typhoid patients subsequently suffer, may be obviated.

Special systems of treatment.—In addition to the general principles of treatment given above, various systems have been tried which are worthy of notice.

Treatment directed against the temperature.—Antipyretic drugs have been very popular, and are still very generally employed. In our experience, however, they are undesirable. The ordinary fever of a typhoid case runs such a fixed and definite course, that it is hard to believe that the pyrexia is not nature's cure for the disease. Apart from cases where the temperature has become hyperpyretic, we have seen no good resulting from the use of antipyretics. The excuse for their employment is the damaging effect of a continued high temperature upon the cardiac muscle.

If any drug is to be used, quinine is probably at once the safest and the most efficient, and in cases of hyperpyrexia it may be extremely useful. Its dose should vary from 15 to 25 grs., according to the severity of the case. Phenazone, acetanilide, and the whole group of coal-tar derivatives, should be avoided. In the first place, they occasionally cause cyanosis, with dangerous collapse; and secondly, what is more important, they prevent to a large extent the free elimination of the toxines of the disease.

Hydrotherapeutic means have been used with much more success. Of these Brand's system is by far the most important; and although it has never had a fair trial in this country, it has given admirable results on the Continent and in America. The technique of the system consists in immersing the patient in a bath whenever the temperature taken in the rectum reaches 102°·2 F. The bath is not to be warmer than 65° F. A compress, dipped in water of about 5° lower, is placed on the head of the patient, or cold water may be placed over the head and shoulders. Compresses of ice-cold water are placed on the chest and the abdomen. The patient remains in the bath fifteen minutes, during which he is encouraged to rub himself, and is systematically rubbed down by his attendants. This friction is of great importance, and is designed to stimulate the peripheral circulation. About eight or ten minutes after immersion, shivering usually begins, but this is to be disregarded, and the full time prescribed should be occupied in the process. The patient is then removed, wrapped in a coarse linen sheet, over which a blanket is folded, and the extremities are thoroughly dried and rubbed. A little alcohol is then usually administered. The bath is to be repeated every three hours, unless the temperature remains below 102°·2 F. The diet should consist of liquids, and no drugs are given.

In spite of the apparent severity of this treatment, the death rate of typhoid fever has been considerably lowered in all hospitals where it has been systematically used. The great secret of its success would appear to lie in the fact, not that it lowers temperature, but that it promotes elimination. Diuresis is much more free, and the toxines are discharged in much greater quantity. Its danger appears to be the risk of causing shock, in case of weak heart. In such cases it is better to start with a bath at the temperature of the room. The method has been accused of increasing the chances of hæmorrhage, but as the dangerous hæmorrhage of typhoid is always ulcerative, it is not easy to see how it could be affected by external conditions.

Various applications of cold water and ice will be found very useful in high degrees of fever. Cold sponging and cold packing are perhaps the easiest methods to adopt, and usually do very well. Graduated baths, where the water is cooled down from the temperature of the patient, are also effectual in reducing temperature, and have the advantage of avoiding shock.

Another systematic water treatment is that of Barr, who keeps his patients during the whole course of their fever in a tank bath, kept at a few degrees below the temperature of the patient.

Treatment directed against the bacteria and their products.—Drugs.— Various attempts have been made to cut short the course of the fever by the administration of antiseptic drugs. While complete success has not been obtained, many observers have had favourable results. It is obviously impossible to make the bowel aseptic, but it is possible, by the administration of certain drugs, to effectually deodorise the stools. Of

these drugs salol is perhaps the most used, and may be given in doses of 10 grs. every four or six hours. We have had, however, better results with naphthol β, in doses of 6 to 9 grs. every four hours. Guaiacol carbonate also gives good results. Calomel has long been popular in typhoid fever, and is very useful combined with any of the above remedies throughout the course of the whole fever. Other well-known antiseptics are salicylate of bismuth, naphthalin, turpentine, eucalyptus oil, and thymol. Chlorine water is also frequently used.

Of these antiseptics, it may be said that they do not injure the patient, they do not cut short the fever, and they do not prevent relapses. On the other hand, they deodorise the stools, and possibly thus reduce the risks run by the attendants. They may also modify the ulceration, and lessen the severity of the attack.

Antitoxine.—There is yet no true antitoxine for typhoid fever. The serum so called is a bactericidal preparation, but does not probably directly counteract the toxines of the disease. We have not seen much advantage in its use. What will always prevent a very successful serum treatment of typhoid fever is, that it is so pre-eminently a disease which comes late under medical observation. To obtain much effect with any antitoxine, it is necessary to get the cases early.

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J. O. AFFLECK.
CLAUDE B. KER.

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VARIOLA AND VACCINIA.

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Syn., Fr., *Petite vérole ;* Ger., *Blattern* or *Pocken.*
Syn., Fr., *Vaccine ;* Ger., *Kuhpocken.*

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An acute, specific, highly infectious febrile disease, setting in suddenly with chills, headache, vomiting, sweating, salivation, tenderness on pressure in the pit of the stomach, and severe pain in the lumbar and sacral regions. The range of temperature is characteristic: high before the rash appears, it falls with the coming out of the true eruption, to rise again as a secondary fever develops, when suppuration takes place at the end of the first week. There is a specific inflammation of the skin (dermatitis) and often of the mucous membranes also. The dermatitis is shown by the development, usually on the third day, of a papular or pimply rash, which quickly becomes vesicular, and finally, in many cases, pustular. These pustules, in the end, dry up, and form foul-smelling and extremely infectious crusts, which are cast off or shed about the eighteenth day. The disease is not infrequently complicated with hæmorrhages into the skin (*purpuric smallpox*), and from the mucous membranes (*hæmorrhagic smallpox*); these may occur early, and interfere with the development of the true smallpox eruption; or late, constituting *Variola hæmorrhagica pustulosa* (Curschmann). In convalescence a remarkable tendency to the formation of boils and abscesses is observed in the severer cases, especially in those accompanied by a profuse and general rash (*confluent smallpox*).

History.—The origin of smallpox is unknown. Its native foci were most likely situated in China, India, and Central Africa. Its diffusion eastward and westward was probably effected by the Saracen armies at the era of the Hegira, A.D. 622. The name "variola" occurs for the first

time as a designation of the disease in a description by Marius, of an epidemic which was widely prevalent in France, Switzerland, and Italy, in the year 570. The researches of antiquarians lead to the belief that smallpox first appeared in England about A.D. 900. All authors concur in representing the frightful mortality occasioned by this pestilence, and the consequent terror which its visitations everywhere excited. Holinshed, in the sixteenth century, was the first to use the word "smallpox." Writing of an epidemic which occurred in the reign of Edward III., he says: "Alsoe manie died of the *smallpockes*, both men, women, and children." In the Middle Ages, the death toll of smallpox could be counted by millions. Before the introduction of vaccination, just a century ago, the annual mortality from the disease in England and Wales alone was at the rate of 3000 in every million of the population. In 1890 smallpox caused only fifteen deaths in England; and the average annual number of deaths from this disease in the ten years 1881–90 was 1,227·8—that is, only one-seventieth part of the death-rate of pre-vaccination times. Thus great has been the boon conferred upon mankind by the discovery of Jenner.

Etiology.—To Boerhaave belongs the credit of assigning *contagion*
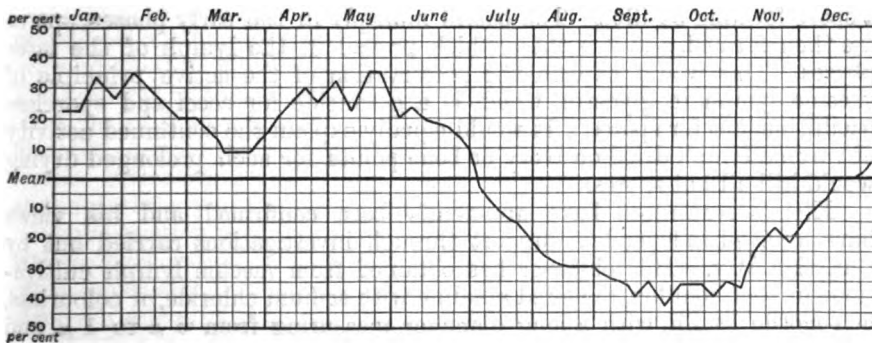
FIG. 11.— Smallpox mortality curve.

as the proper exciting cause of smallpox. Outbreaks of the disease occur periodically, over wide districts or in localities of limited area, and independently of climate, soil, or race, whenever the contagium, virus, or essential poison of smallpox is introduced among a population open to its reception; that is to say, a population unprotected by a previous visitation, or by inoculation, or by vaccination. Although smallpox is apparently independent of climate, yet the season of the year has a marked influence upon its prevalence. It is essentially a disease of winter and spring. In the British Islands and Western Europe generally, for example, the monthly number of cases is high from November onward; but from May a rapid decline in the prevalence of the disease takes place, the least number of cases being observed in September. The critical mean temperature in regard to smallpox appears to be 50° F. When the mean falls below that value, the disease spreads; when it rises above it, the disease wanes. The explanation is no doubt to be found in the fact that defective ventilation, overcrowding, and deficient nutrition, wait on cold weather, and these are the most powerful predisposing causes of smallpox no less than of typhus fever.

The curve, Fig. 11, based on the returns for London of the Registrar-

General for England during the fifty years 1841–1890, clearly illustrates the seasonal prevalence of smallpox.

Individual susceptibility to the poison of smallpox extends to the whole of mankind, but experience shows that the coloured races, and particularly the negro race, are—other things being equal—in greater risk from smallpox than the whites.

Turning from the predisponents of the disease to its *causa causans,* or *exciting cause,* we are led by analogy to regard the virus as microbic in its nature, although we are obliged to admit that the bacteriology of smallpox is still incomplete. Klein has described a peculiar and extremely minute bacillus, or rod-shaped micro-organism, as occurring in the calf lymph and in human variola lymph during the early phases— in the calf lymph, seventy-two to ninety-six hours after vaccination; in the human variola, during the third or fourth day. In both instances the lymph was collected aseptically. In the bacilli—when abundant— forms were recognised in which some globules resembling spores existed. Calf lymph of later stages (five or six days old) showed no bacilli, or only here and there a trace. The presence of these spore-like bodies, and the absence of bacilli in the lymph of later stages, led Klein to conclude that in smallpox and the vaccine disease we have to deal with a spore-forming bacillus. The bacilli multiply in the early phases, spores are then formed, and it is these which prevail in the lymph of the later phases. This would explain the preservation of the active principle of vaccine lymph in glycerin, which is a germicide for cocci and sporeless bacilli, but not for spores. It would equally explain the continued activity of vaccine lymph dried on ivory or bone points, for such prolonged drying would kill all but spores.

Klein's researches have apparently been confirmed, and his views have received independent support through investigations carried out by Christian Bay. This observer has obtained from vaccine lymph cultivations in beef bouillon, rendered alkaline with sodium chloride, of colourless, non-motile bacilli, with a long diameter measuring from $\cdot6\ \mu$ to $1\ \mu$, and the short diameter from $\cdot2\ \mu$ to $\cdot3\ \mu$. These organisms were found, with three exceptions, in examinations of sixty-five cultures from vaccine points. These bacilli bear spores from an early stage of their development. The organism contains two spores, one at each end. As this is the most conspicuous feature of the organism, Bay refers it to the genus *Dispora,* and calls it *D. variolæ.* The same organism was also found in the lymph from a case of confluent smallpox in the Smallpox Hospital, Chicago. Of forty cultures in bouillon made from this lymph, only two failed to show the presence of Bay's bacillus.

Smallpox is a typically infectious disease. Most usually it spreads from person to person. It clings to articles of furniture or of dress, which therefore act as *fomites,* or carriers of the infection. It may be conveyed through the medium of an individual, not himself ill·of it, as in a striking case reported by Hewitt. It may be acquired from the dead body. Watson tells that the corpse of a man who had died of smallpox was brought into the dissecting-room, with the result that four students took the disease. As Hirsch graphically puts it, "an atmosphere of smallpox poison develops around the sick, especially when they are crowded in close rooms." In other words, "the air may become a carrier of the contagion, so that the latter can be spread by the atmospheric currents within a small range." Although Hirsch thought that no mathematical expression

could be found for the extent of that range, and that, at the utmost, it went no farther than the immediate surroundings of the sick, yet the experience of recent epidemics in the British Isles proves that the *striking distance* of smallpox is considerable—certainly much greater than that of typhus fever. In the Sheffield outbreak of 1887–1888, the infecting influence of the smallpox hospital could be distinctly traced along a radius of 4000 feet. Wynter Blyth observes that this possibility of smallpox spreading by aerial infection increases greatly both the hospital difficulty and that of individual isolation. There can be no doubt that the chief stages of infectiveness in smallpox are the earliest period of suppuration, and the stage of desiccation, crusting, or scabbing.

Morbid anatomy and pathology.—As regards the skin, Unna shows that the poisoned epithelium in the upper prickle layer of the rete mucosum softens, becomes œdematous from swelling of the protoplasm within the epithelial cells, while a secondary coagulation of the albuminoid bodies, set free from the epithelial protoplasm, takes place, constituting a fibrinoid degeneration of the epithelium. In smallpox, this advances slowly —much more slowly than in chickenpox—and is quickly followed by sup-puration. This arises partly from intense inflammation, partly from a secondary infection of the skin by pyogenic micro-organisms.

Owing to the slow advance of the colliquation, or softening of the prickle cells, other epithelial cells are compressed into trabeculæ, or septa, perpendicular in the centre, and directed somewhat outwards at the sides. The younger epithelial cells of the lower prickle layer meanwhile assume the form of hollow spheres or balloons. Unna accordingly describes the fibrinoid degeneration of the epithelium in smallpox as presenting two forms—reticulating and ballooning colliquation. The first predominates at the periphery of the pock; the second at its centre.

Umbilication is to be ascribed, in the vesicular stage, in part to reticu-lating degeneration, in part to epithelial œdema. Of these, the former is often especially developed at the periphery of the pock; the latter is always limited to the periphery. The less swollen centre, where ballooning colliquation predominates, simply remains behind. Unna admits that, where a hair follicle accidentally runs through the centre of the pock, a form of depression may be produced, for the swelling of the prickle layer will here be limited by the cornified neck of the hair follicle. But this exceptional case does not explain the characteristic central depression of the smallpox vesicle. This depends on the two changes in the periphery of the pock, which have been named reticular colliquation and œdematous swelling of the epithelium, while ballooning degeneration or colliquation leads only to a very slight increase in the centre of the vesicle. Hence the periphery is prominent; the centre is depressed, and apparently retracted.

From the fifth day onward, the blood vessels throughout the cutis are dilated. A full stream of leucocytes causes an ever-increasing infarction or plugging of the vesicle or pustule, which is thus converted into an almost solid tissue; or, if the horny layer of the cutis yields, a more or less profuse suppuration lasts for a time, or speedily ends in the formation of a crust or scab. When the scab is thrown off, a persistent, trough-like depression is displayed. The depth of the scar depends on the degree and the duration of the flattening of the base of the pock beneath the pustule and the scab. Hence Unna says that "the rational treatment to avoid scars should be mainly directed to the aborting of the pustular stage, and the rapid removal of the scab by profuse epithelial new growth."

The liver, kidneys, spleen, and heart muscle undergo important morbid changes. The spleen swells; its pulp becomes soft, and of a light-red colour. The liver, kidneys, and heart muscle are the seat sometimes of cloudy swelling (granular degeneration), sometimes of acute fatty degeneration, resembling that produced by poisoning with phosphorus. In malignant smallpox, large or small hæmorrhages may be found in nearly all the viscera, ecchymoses in the serous membranes, and extravasations of blood in almost all the mucous membranes.

Symptomatology—Stages.—The course of smallpox may be divided into five stages—incubation, invasion, eruption, secondary fever, desiceation, and desquamation.

Incubation.—This begins with the reception of the virus into the system, and ends when the earliest symptoms appear. Its average duration is twelve days inclusive, except after inoculation, when it is only eight days or less. A familiar example of the process is the everyday practice of vaccination, or the engrafting of the vaccine disease by puncture of the skin, and the insertion into the wound of vaccine lymph. As a rule, there are no symptoms in this stage, which is therefore called the latent period. Towards its close, however, the patient feels unwell and out of sorts.

Invasion.—Smallpox sets in suddenly and with violence. The earliest symptoms are connected with the nervous system. They are: chills, rigors, and—in young children—convulsions; lumbar or sacral pain, from hyperæmia of the spinal cord; pain in the pit of the stomach, nausea, and often vomiting, severe headache, delirium, rheumatoid pains in the limbs. There is constipation, except in children, in whom diarrhœa, sleepiness or drowsiness, and stupor may occur. Constant profuse sweating is usual. There are, besides, loss of appetite, thirst, furred tongue, very fœtid breath, full and rapid pulse, and prostration. In women, menstruation nearly always comes on, whether the period is due or not, and it is generally profuse. All these symptoms are apt to be more acute and persistent in confluent than in discrete smallpox.

On the first or second day the temperature rises quickly to 104° F. (= 40° C.), seldom below this point, sometimes above it—even to 105°·8 F. (= 41° C.). The maximal temperature is usually reached shortly before the rash appears on the third day. This initial fever is called the prodromal fever, because it thus runs before or precedes the appearance of the eruption.

During this stage *accidental rashes* are apt to appear, causing much difficulty in diagnosis. They are usually erythematous in character—if diffuse, resembling scarlatina or erysipelas; if spotty, or macular, resembling measles. This prodromal or initial erythema is called *roseola variolosa*. It is very evanescent, and may usher in an attack of varioloid or modified smallpox; and so it has no little prognostic value. It probably depends on a reactive inhibition of the vasomotor system of nerves, brought about by the fever poison. Parts of the body affected by a roseola variolosa may afterwards remain free from the true smallpox rash. A more serious sign is the development, even at this early stage, of petechiæ, or extravasations of dissolved hæmatin under the skin, varying in size from a pin's head to a pea or a bean. These purpuric rashes are commonly seen on the sides of the chest or over the lower part of the abdomen and the inner aspect of the thighs—the brachial and crural triangles. The stage of invasion lasts on the average for three days; as a rule, it is prolonged

in the milder, shortened in the severer cases, so far as the amount of the true rash is concerned. This rule may be accepted as a sound working proposition, although there is one striking exception to it. In consequence of great organic lesions, the eruption may be retarded till the sixth or seventh day in both discrete and confluent cases. A purpuric or hæmorrhagic tendency early in smallpox postpones, it may be indefinitely, the showing of the true rash

Eruption.—The true rash of smallpox appears first on the head, face, and neck, and about the wrists, next on the trunk, and lastly on the lower extremities. The usual time for its appearance is the third day inclusive from the earliest symptoms. In confluent cases it may show itself on the second or even on the first day; in discrete cases its coming may be postponed until the fourth day.

The "pocks" appear on the first day of the rash as points of hyperæmia, like the fine pricks made with a needle, or like recent flea-bites. Owing to changes in the rete mucosum and to cell proliferation, a papule or pimple quickly forms. This is slightly raised, conical, and hard, feeling like a grain of shot beneath the skin—it feels shotty on the second and third days of the rash. Exudation of serum soon takes place, so that the horny layer of the epidermis is raised to form a vesicle. Its contents, clear at first, soon become opaque, lactescent or milk-like, on the fourth and fifth days of the rash. Pustules or small abscesses are then formed through further changes in the vesicles, in which young cells increase and multiply, their contents becoming yellow and purulent on the sixth and seventh days of the rash. About this time also a central depression or dimple is found in these pustules, owing to epithelial œdema at the periphery of the pock. This is the so-called umbilicus, at the bottom of which the opening of a hair follicle or sweat gland is, according to Curschmann, frequently seen. The variolous inflammation is not confined to the epidermis. The papillary layer of the derma is often involved, its connective tissue elements proliferate and afterwards undergo cicatricial contraction, leading to the permanent deformity known as "pitting." A person is then said to be "pock-marked."

The period of fullest development of the rash is reached on the seventh day from its appearance—the tenth day, inclusive, of the disease. Each pustule is now surrounded with an inflammatory zone or areola, called its halo. This period is called the period of maturation or ripening. It lasts about three days, and is followed by the last stage in the life-history of the eruption, that of desiccation—the rupture and drying up of the pustules, and the formation of foul-smelling crusts or scabs.

Desiccation.—A yellowish matter, like thick honey, oozes from the surface of the pustules. This, with the pus or serum, speedily dries up, first in the centre; and brownish scabs form, which are at first adherent, but afterwards fall off in from three to six days, leaving elevations or projections of a violet-red hue, like a cold skin. With the drying up of the pustules, the redness, swelling, and tenderness of the skin subside, the eyes reopen, the nostrils are cleared, and the features of the patient become once more recognisable.

Desquamation.—After the eighteenth day, or so, of the attack in confluent cases, successive scales of epidermis form and peel off—a process which is called desquamation, or scaling—ultimately leaving a small white puckered scar, or "pit," should the variolous inflammation of the skin have dipped deep and involved the papillary portion, or *cutis vera.* When

every scab has fallen off, and desquamation has ceased, the patient may be considered free from infection.

The rash of smallpox is by no means confined to the skin. A true variolous exanthem or endanthem develops upon the mucous membranes in general. The conjunctivæ, the mucous membranes of the nose, mouth, pharynx, and adjacent parts, are nearly always affected. The rash may thence extend through the whole system of mucous membranes, invading the larynx, trachea, and bronchi in one direction; the œsophagus, stomach, and intestines in another. Thence arise many of the more serious complications of smallpox. The eyes and eyelids are inflamed, and sight may be lost. We may have deafness, due to blocking of the œdematous Eustachian tubes; hoarseness or aphonia; cough and dyspnœa, from bronchitis and pneumonia; dysphagia, or difficulty of swallowing; diarrhœa; colitis. According to Curschmann, true pocks upon the serous membranes are fables belonging to antiquity.

Varieties.—A classification of smallpox, based upon the distribution and amount of the rash, has been handed down from the time of Sydenham, and has received universal acceptance.

Whether modified or unmodified by a previous attack or by vaccination, smallpox appears under two principal forms—discrete and confluent. The first of these is generally free from danger; the latter is one of the most terrible, loathsome, and fatal of diseases. Of confluent smallpox, two modified varieties are described, namely, semiconfluent or coherent smallpox, and corymbose smallpox.

Variola discreta vel distincta is the name given to those cases in which the rash is sparse or scanty, the several papules or pustules being more or less widely separated from each other; hence the term *discrete*. In this form the initial symptoms are, as a rule, less acute and less persistent, and the rash not infrequently stops short of the pustular stage (*V. crystallina*).

Variola confluens is the term applied to those cases in which the rash overruns the entire, or nearly the entire, surface of the body, and invades the mucous membranes also with great severity. The invasion symptoms are all intensified, and the rash appears as early as the second day. In this dangerous variety the following characteristic symptoms are often present: —Persistent diarrhœa; profuse salivation, either from parotitis, or as a reflex symptom from stomatitis (inflammation of the mucous membranes of the mouth); great swelling of the face and eyelids, so that the latter sometimes burst or slough; most painful swelling of the hands and feet; delirium—sometimes busy with extreme muscular agitation, often violent, noisy, homicidal, or suicidal. In this variety of the disease, the pocks are pale, crude, pitted, and *sessile*. The face is covered with pustules, which run together, so that the epidermis is raised by a milky purulent secretion, and the face seems as if it were dipped in tallow or covered with a parchment mask.

While the face and hands may be absolutely covered with pocks, the eruption may be more or less discrete in other parts of the body, the amount and intensity of the pustulation seemingly bearing a direct relation to the vascularity and inflammatory state of the surface. The mucous membranes, like the skin, are the seat of a closely-set rash in confluent smallpox, and very dangerous forms of secondary inflammation are apt to place the patient's life in imminent peril. Towards the close, should the patient survive, multiple pyæmic abscesses, erysipelas, and even gangrene, may

occur in those parts of the integument where the confluence is most pronounced.

The mortality is of course very great in this form of the disease, at any stage of which the patient may succumb. Confluent smallpox is the most deadly of all pestilences, yellow fever and cholera not excepted. The most fatal epoch is about the eleventh or twelfth day, but even far on in the stage of desiccation death not seldom results from exhaustion, or pyæmia, or some other complication.

Should confluent smallpox end in recovery, convalescence is very tedious, and is often interrupted by serious sequelæ, of which an "acute furuncular diathesis," as Trousseau called it, is one of the commonest and most trouble-some. It shows itself in the formation of successive crops of most painful boils and carbuncles, and of more or less deep-seated abscesses. In the stage of desiccation, also, large, foul, ecthymoid crusts may form upon the ulcerated surface of the skin. With the separation of the scabs, or some-times later, the hair commonly falls off, at times in handfuls. The resulting alopecia, or baldness, is occasionally permanent.
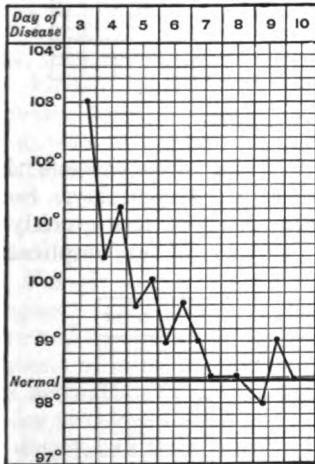
FIG. 12.—Discrete smallpox.
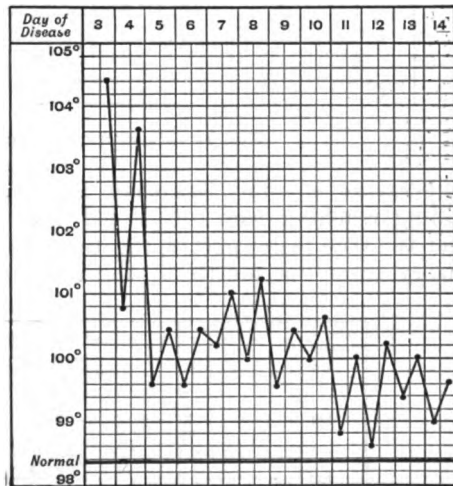
FIG. 13.—Discrete smallpox.

Variola semiconfluens, or *coherent smallpox*, is where the pustules touch each other without coalescing, or the eruption is confluent on and about the face, and more or less discrete elsewhere.

Variola corymbosa is a term applied to those cases where the pustules are confluent in patches or clusters, these being separated by intervals of unaffected skin. Vascular parts, like the armpits, groins, and popliteal spaces, are often the seat of such a rash. According to Marson, this is a very fatal variety of smallpox, the mortality reaching 41 per cent. Strangely enough, it was scarcely less destructive to vaccinated persons than to those who were unprotected.

Temperature.—The symptomatology of smallpox would not be complete without at least a brief account of the behaviour of the body temperature in the disease. The accompanying charts (Figs. 12–16) have been selected to illustrate the varying grades of intensity of the fever movements in smallpox. Two distinct fever types are observed. The prodromal or initial fever of the stage of invasion is a brief continued fever, which is

often very severe, even in the mildest cases of variola discreta, and of varioloid or modified smallpox. In these forms the prodromal fever both begins, and commonly completes, the febrile movement. Its maximal
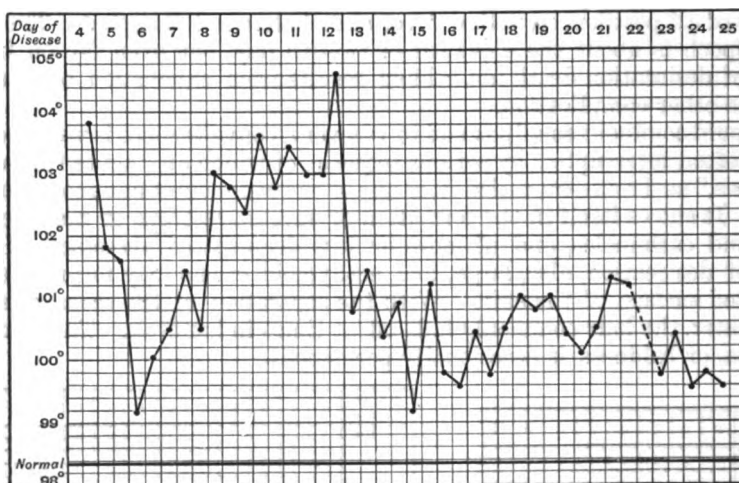
Fig. 14.—Coherent smallpox—secondary fever.

temperature is rarely less than 104° F. (40° C.), and often exceeds this reading, reaching even 106° F. (41°·1 C.) as early as the second day. Soon after the true rash appears, the temperature falls more or less quickly— usually from the fourth to the sixth day. In cases of uncomplicated
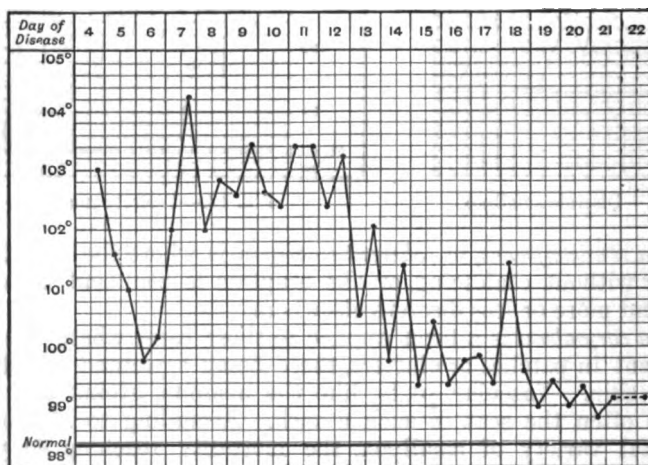
Fig. 15.—Confluent smallpox—severe secondary fever.

varioloid, and of mild, discrete smallpox, this defervescence, or cooling down, is complete and final.

The fall of temperature which occurs with the coming out of the rash of smallpox is pathognomonic of this disease. It is exactly the converse of the behaviour of the temperature in measles, in which the fever is moderate

up to the appearance of the rash, and then becomes more and more intense, until the rash is most fully developed.

The other type of fever in smallpox is relapsing in character. It occurs in the severer and confluent forms, in which the defervescence of the eruptive stage is incomplete. In other words, the initial fever runs on, until, with the beginning of pustulation, or maturation of the rash, the temperature again begins to rise, ushering in a secondary fever—the fever of suppuration, or of maturation. This secondary febrile movement is of indefinite duration, and varies in intensity in proportion to the severity of the attack. There are morning remissions, and evening exacerbations of temperature, with occasional *spikings,* or isolated extreme elevations. Readings above 104° F. during this fever of suppuration are a sign of danger, and, in fatal cases, hyperpyrexial temperatures (107°·6 F.=42° C.) are wont to occur before, at the moment of, or even after, death. In cases which tend towards recovery, defervescence takes place by an irregular lysis, or gradual resolution of the fever, as opposed to crisis, in which temperature falls briskly and permanently

Apart from discrete and confluent small-pox, we meet with the following varieties:—

Variola benigna, or *varioloid*—a mild and abortive form, in which the pocks either fail to appear at all, or else fail to pass through the later stages of their development, stopping short at the papular stage; or, if reaching the vesicular stage, drying up and shrivelling on the fifth or sixth day of the eruption.

Variola maligna— V. purpurica vel hæmor-rhagica.—Apart from confluent smallpox, in which the patient's life is endangered by the amount of suppuration, and the intensity of

Fig. 16.—Malignant smallpox.

the secondary or suppurative fever, malignant smallpox presents itself under two forms—purpuric, and hæmorrhagic. These forms differ merely in degree; in both the blood is profoundly altered, and the characteristic rash of smallpox fails to appear at all, or to run through its several stages.

In the purpuric variety the dissolution of the blood leads to the formation of petechiæ, vibices, or purple streaks and blotches, and ecchymoses. Klebs and Unna, however, attribute these changes to blocking of the vessels of the skin by bacteria.

In hæmorrhagic smallpox, hæmatolysis is carried still further. The ill-fated patient bleeds from every pore and orifice of the body. There is chemosis—he may even weep tears of blood. There is epistaxis—he bleeds from lips and gums. He spits, or coughs up, or vomits blood. The motions from the bowels are tarry. Blood pours from the kidneys, and, in the female, from the generative organs. The tongue looks as if it were parboiled, and there is an unquenchable thirst.

One of the most extraordinary, as well as the most painful, features of this deadly malady is the clearness of mind which often remains with the unhappy patient almost up to the time when he draws his latest breath. There is, in some of these cases, no delirium, no stupor, no dulling of the intellect whatever; the victim literally looks death in the face in full possession of his senses.
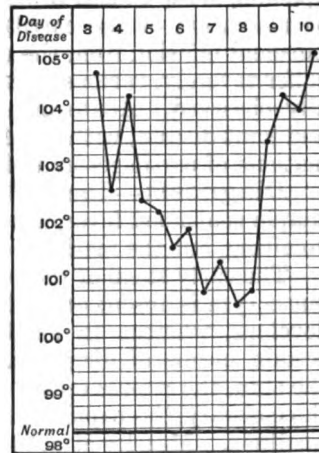
Strong, muscular men, and pregnant, or recently-delivered women, are said to be particularly liable to fatal hæmorrhagic smallpox. Hæmorrhagic or purpuric symptoms occasionally supervene during the eruptive stage. The true exanthem may indeed become the seat of hæmorrhage in its papular, vesicular, or pustular stage, first and especially on the lower extremities. This is the *V. hæmorrhagica pustulosa* of Curschmann, long ago described by Sydenham as Anomalous, Irregular, or Black Smallpox (*V. nigra*).

Sequelæ.—The complications and sequelæ of smallpox are many and often severe. Multiple abscesses and boils may involve the skin, constituting the "furuncular diathesis" of Trousseau. The eyelids may suppurate or slough; atrophic keratitis, iritis, panophthalmitis, or retinal hæmorrhage may endanger or destroy sight. Œdema of the glottis, ushered in by aphonia, often causes death about the eighth day. Laryngitis may lead to ulceration of the cartilages. Bronchitis, pneumonia, or pleuritis, with purulent effusion from the outset, may occur; and the nervous system may suffer severely, various paralyses or disseminated sclerosis being occasionally observed. Acute mania sometimes follows. Pyæmia, or septicæmia and joint disease, with painful swellings, effusions of serum or pus, inflammations of cartilages and of bones, may occur.

Diagnosis.—The prodromal fever of smallpox may be mistaken for simple continued fever, which has no rash, or for scarlatina because of the vomiting, but the marked sore throat of the latter disease is wanting.

The early stage of the smallpox rash closely resembles that of measles, but coryza is absent or slight. In measles, also, fever increases as the rash develops, whereas in smallpox it subsides. The "Grisolle sign" is a certain means of diagnosis. If, upon stretching an affected portion of the skin, the papule ceases to be felt, the rash is that of measles; if, on the contrary, the papule is still felt, hard and shotty, the rash is that of smallpox. Measles attacks children; smallpox, as a rule, adults. The pain in the back is wanting in measles.

The onset of smallpox often closely resembles that of typhus; but the fever persists, and the rash is macular rather than papular in the latter disease. The clinical history should solve the question of a pustular syphilide or smallpox, of glanders or smallpox, and of erysipelas or smallpox. The differential diagnosis of variola and varicella (chickenpox) had best be postponed until the latter disease has been described.

Prognosis.—The mortality depends on—the patient's state as regards previous protection by an attack of natural smallpox, by inoculation, or by vaccination; the virulence of the disease itself—the hæmorrhagic form being the most deadly, next the purpuric form, then the confluent form; the general hygienic condition, or otherwise, of the patient's surroundings; the presence or absence of complications or sequelæ.

Smallpox is most deadly to unvaccinated children under 5 years of age, and to unvaccinated adults over 30 years. Of the confluent cases, 50 per cent. perish; of the most malignant cases, 100 per cent. The influence of vaccination for good is unquestionable—the mortality being 50 per cent. among the unvaccinated in general, 26 per cent. among the badly vaccinated, and only 2·3 per cent. among the efficiently vaccinated.

Hæmorrhagic or malignant smallpox may kill in four, five, or six days from the onset. In confluent smallpox, on the contrary, the patient seldom dies before the eleventh day—the most fatal epochs being the twelfth, thirteenth, and fourteenth days.

Defective sanitary surroundings—such as overcrowding, want of ventilation, bad house drainage—enormously increase the patient's risk.

The complications and sequelæ often kill a patient who may have escaped the perils which beset him in the earlier stages of the attack. Œdema of the glottis, inflammation of the cartilages of the larynx, bronchitis, pleurisy, or diarrhœa, may kill straight off; while pyæmia, septicæmia, and the furuncular diathesis may exhaust the patient's strength after weeks or months of suffering.

Treatment.—This naturally falls under two headings — preventive and curative treatment.

Prophylaxis.—The principles of the preventive treatment of smallpox are based upon two facts in the natural history of the disease—it is eminently communicable, one attack usually protects an individual from a second attack—in other words, it confers immunity upon him. The preventive measures which call for remark are—isolation of the sick, inoculation, vaccination.

Isolation consists in the removal of the sick to suitable epidemic hospitals, the providing of refuges for the inmates of infected tenement houses or other dwellings, efficient disinfection, and the establishment of convalescent homes.

As regards *Inoculation*, the intention was to engraft a mild form of smallpox on a healthy individual, whose receptivity or susceptibility might be supposed to be slight or low in consequence of his existing good health. The disadvantages of this procedure were that it gave smallpox to many who would otherwise have perhaps escaped the disease altogether, while it was not possible to guarantee that the resulting attack of smallpox would be mild. Inoculation is now illegal in Great Britain and Ireland.

Vaccination.—About the middle of the eighteenth century, the opinion gained ground in England that inoculation with cowpox lymph protected from smallpox. It is necessary to explain that various domestic animals are liable to a disease which is practically smallpox. Cowpox is an instance. In this affection the eruption is almost exclusively observed upon the udder and teats of the cow. The malady is technically called *Variolæ vaccinæ*, or shortly *Vaccina* (less correctly *Vaccinia*). Dairymaids and farm-labourers were liable to sores upon their hands, which seemed to arise from contact with pustules on the udders of milch cows. Those who suffered from this apparently local malady of sore hands were observed to escape smallpox. In 1771, a schoolmaster in Holstein, named Platte, is reported to have practised vaccination. In 1774, Benjamin Jesty, a Gloucestershire farmer, inoculated his wife and two sons with cowpox, thus performing vaccination for the first time in this country. On May 14, 1796, Edward Jenner "vaccinated" a peasant lad, whom he failed to inoculate with smallpox two months afterwards. Such was the beginning of vaccination.

Vaccinia.—The symptoms of *Cowpox*, or the *Vaccine Disease*, are first local, then constitutional. At the site of inoculation with vaccine lymph, which may be bovine or humanised—that is, derived from the calf or heifer, or from a human being already vaccinated—a patch of redness appears on the third day inclusive. This rapidly develops into a papule or pimple, which in its turn, about the fifth day, becomes surmounted with a pearly vesicle, multilocular, oval, or circular in outline, with raised margin and depressed centre. This vesicle enlarges until the eighth day, its contents increasing but remaining clear as crystal. An inflammatory red zone, called the areola, now develops, spreading out from the base of the vesicle to a

distance of perhaps two or three inches. After the tenth day the areola fades, the vesicle shrinks and dries up in the centre, while the contained lymph becomes opaque, and thickens. By the fourteenth or fifteenth day a hard, dry brown scab forms, which finally separates and falls off about the twenty-first day. A circular, slightly depressed, foveate or pitted scar remains, which is generally permanent through after-life.

The constitutional symptoms are—slight feverishness from the fourth day, becoming more marked from the eighth to the tenth day; often derangement of the stomach and bowels during the stage of areola, with restlessness. The axillary glands may swell and rashes may show upon the skin—either a blush, or a crop of papules, or a vesicular rash. These symptoms subside in a few days, or fail to appear at all.

Vaccination in rare instances has done harm. Unsuitable subjects have been vaccinated, or impure lymph has been used. The syphilitic virus has been inoculated along with vaccine lymph, giving rise to *vaccino-syphilis*, the most deplorable accident by which carelessness or misfortune can prejudice the performance of vaccination. Such mishaps, however, afford no valid argument against the practice of vaccination.

The circumstances which conduce to the success of the operation are these—

The subject to be vaccinated should be healthy, neither teething nor being weaned.

The vaccinifer should also be healthy, vaccinated for the first time, and above all free from any syphilitic taint.

The lymph should be taken not later than the eighth day.

The incisions, punctures, or scarifications should not penetrate to the subcutaneous areolar tissue. They should be made with a scrupulously clean or sterilised instrument, the skin having been first washed and sterilised as far as possible.

Bleeding should be avoided, lest the lymph be washed away from the site of inoculation.

Lymph which has been drawn from a vesicle already showing the areola should not be used. This is Jenner's "golden rule."

Thin, serous, readily flowing lymph should not be used. Good lymph is perfectly limpid and viscid or sticky.

Curative treatment.—No specific for smallpox has yet been discovered. The two great principles of treatment are—to guide the essential disorder to a favourable termination, and to combat secondary affections as they arise.

Discrete smallpox.—The patient, having been placed in bed in a large, airy, and well-ventilated but warm room, should be carefully and skilfully nursed. His hair and beard should be cut close, his face and hands should be washed daily, or twice a day, with warm carbolised water, from 1 to 2 per cent. in strength, or with creolin and water, or with a weak solution of corrosive sublimate (mercuric chloride, 1–2000). Warm baths are very useful and refreshing. The water may with advantage be tinged with permanganate of potassium solution, unless soap is used. Lindholm employed with complete success the method recommended by Finsen, of treating smallpox patients in a room from which the ultra-violet rays of the solar spectrum are shut out by red window panes, or by covering the windows with red curtains. The eruption dried up shortly after its appearance, no fever of maturation took place, and the patients recovered quickly, having but few scars, even when at first severely attacked.

Confluent smallpox.—The pain in the back is relieved by dry-cupping, by applying an indiarubber bag filled with hot water, or by a hypodermic injection of ergotin. To check the development of a copious eruption, the red-light treatment may be adopted. In quinine and in perchloride of iron we possess the two most valuable antiseptics for internal use. Three important indications for treatment, so far as the rash is concerned, are—the exclusion of air; the keeping of the skin in a permanently moist state, so as to prevent the hardening of the scabs; the lessening of the local irritation. Many suggestions have been made to fulfil these indications. My own plan is to apply over the face a light mask of lint, thoroughly soaked in a mixture of iced water and glycerin (a teaspoonful in an ounce of water), and covered with oiled silk. Similar dressings may be applied to the hands and feet.

Closely akin to this plan and like measures, is the treatment by the warm or tepid bath. Hebra appears to have had his attention drawn to this method of treatment through observing its efficacy in the management of extensive burns. Stokes strongly recommended the continuous warm bath as a palliative in the delirium and pain of confluent smallpox. He held also that marking or pitting seldom occurred when the surface was protected from the air from an early period, and kept in a permanently moist condition. The continuous warm bath fulfilled the three important indications of treatment above mentioned, and that, too, as regards the entire person of the patient.

The treatment of such skin affections as bedsores, abscesses, boils, erysipelas, and gangrene, consists largely in scrupulous cleanliness and efficient nursing. The body linen should be frequently changed. The patient should rest on a water-bed, or a woven wire mattress. If the feet and hands are wrapped in wet cloths, covered with oiled silk or gutta-percha tissue, the intense pain which attends the formation of pustules upon the soles of the feet and palms of the hands will be avoided.

The eyelids should be poulticed, or kept covered with cold compresses, to reduce œdema. Lint moistened with glycerised water (one teaspoonful of glycerin, or of glycerin of carbolic acid, to a saucerful of tepid water) is an excellent application. For atrophic keratitis, cod-liver oil, iron, wine, and good food are indicated.

Affections of the mouth, tongue, and pharynx are best treated with ice and antiseptic sprays or gargles. In cases of laryngitis, ice is invaluable internally. It may also be applied to the neck externally. Hot poulticing also often gives relief, or fomenting the neck with sponges wrung out of hot water. The steam-kettle should be kept going, and the patient should be placed in a croup tent, and plied with food and stimulants at short but regular intervals.

Diarrhœa is often controlled by a starchy diet, with milk sterilised by boiling, by exhibiting brandy or port wine, and by poulticing the abdomen. Salicylate of bismuth, salol, or carbonate of guaiacol will be found useful. Solution of pernitrate of iron may be prescribed, or pills of acetate of lead and opium, or, in the case of children, aromatic chalk powders. Ten drops of glycerin of carbolic acid and ten drops of tincture of chloroform and morphine are an excellent combination, given at intervals as required. For children the dose should be lessened according to age.

While it too often happens that all our efforts to combat hæmorrhagic smallpox are in vain, yet we may save life by the administration of the solution or tincture of ferric chloride in full doses—30 minims every third

hour, or of gallic or tannic acid in 5- to 10-gr. doses, or of turpentine and ergot, or of liquid extract or tincture of hamamelis in full doses. In menorrhagia and metrorrhagia, also, cold applied to the vulva is of use, or slapping the buttocks with cloths dipped in ice-cold water. Hot water may be injected into the vagina with advantage.

In these awful cases stimulants are imperatively called for—brandy, whisky, or wine, according to circumstances, and especially egg-flip and turpentine punch. Inhalation of oxygen should be tried, and perhaps transfusion of blood, as recommended by Curschmann.

<div align="right">J. W. MOORE.</div>

VARICELLA—CHICKENPOX.

Syn., Ger., *die Wasserpocken, die fliegende Blatter* ; Fr., *Petite vérole volante* ; Old Eng., *Waterpox or Glasspox* ; Scot., *Crystalpox.*

An acute, specific, very infectious febrile disease, especially of infancy and early childhood, not dangerous to life, characterised by the appearance on the skin of successive crops of clear, colourless, watery vesicles. It is a separate and distinct disease from smallpox. The accompanying fever is usually moderate and remittent in type, increasing and abating as the vesicular rash comes and goes.

History.—About 1550, two medical writers, Vidus Vidius and Ingrassias of Naples, described the disease under the name *Crystalli*, owing to the clear, crystalline contents of the vesicles. The malady was first fully described in England by Heberden in 1766, under the name of *Variolæ pusillæ*. Two years previously, Vogel is said to have introduced the term "Varicella," which, like "Variola," is a diminutive of the Latin *varus*, a pimple. Heberden pointed out that it was important to recognise chickenpox, because those who had it might otherwise be deceived into a false security, which might prevent them from keeping out of the way of the smallpox or from being inoculated.

Etiology.—Chickenpox is essentially a disease of childhood, and usually occurs before the first dentition is completed. Even sucklings may be attacked, but among children over 10 years of age the disease is infrequent. Nevertheless, many instances are on record of adults contracting the disease. In 1889 a friend of mine, æt. 25 years, himself a member of the medical profession, had in Dublin a well-marked attack; and in 1894 a gentleman, æt. 32, passed through a typical attack under my observation.

Chickenpox shows itself sporadically, or in moderate and often-repeated local epidemics quite independently of smallpox. Its appearance is not determined by season, but it often follows in the wake of other specific fevers—notably scarlatina.

The intimate nature of the specific virus of varicella is as yet unknown. It is supposed that the virus is generally inhaled. Only rarely can it be inoculated. Its tenacity of life does not seem to be great. In marked contrast with the practical non-inoculability of chickenpox, is the facility of its dissemination among little children by contagion. As a rule one attack confers a lifelong immunity on an individual.

Morbid anatomy and pathology. — According to Unna the

varicellous process commences with the reticulating liquefaction of a few prickle cells of the central and upper prickle layer, in the middle of the first-appearing congestive spot. The completely liquefied, confluent cavities rapidly dilate to form the vesicles; the persistent non-liquefied epithelium is compressed to form the septa, as are the cells above to form the cover of the conoidal, or tent-shaped, vesicle. Its contents, at the height of its development, consist of finely granular, coagulated fibrin, enclosing a few fibrinously degenerating, compressed, or ballooned epithelial cells, and scarcely any wandering cells.

The acuteness which distinguishes the varicellous process is evident histologically (in distinction to smallpox) in the relatively large, slightly septate cavities, due to the rapid distension of a few liquefied cells. Notwithstanding its appearance, the chickenpock is certainly not monolocular. Its thin covering and superficial position result from rapid formation.

The non-purulent character of chickenpox is histologically very pronounced. "Its benign, unscarred course," Unna says, "is explained by the superficial position, the absence of purulent infection of the vesicle, and the early repair by young epithelium, indicated by the numerous mitoses around the cavity. The absence of a dimple results from the acute, abortive course of chickenpox, which does not permit the formation of a swollen peripheral zone of reticularly degenerated and very œdematous epithelium."

Symptomatology.—The stage of incubation or latency is thought to be on the average about as long as that of smallpox, namely, twelve days. Towards the close of this stage there is, according to Thomas, in some cases a slight rise of temperature.

The state of invasion is badly marked. The child often feels perfectly well until the rash appears or is accidentally discovered. In other cases, malaise, loss of appetite, a feeling of sickness, headache, chilliness, and muscular pains, precede the rash by a few hours, or one to even three days. The prodromal fever is usually slight—sometimes a sudden rise of temperature to 101°, or even to 104°, takes place just before the rash comes out.

The stage of eruption may be ushered in by a roseolar, scarlatiniform rash, but the true rash consists of papules or macules, like the rose spots of typhoid fever, fading on pressure, and rapidly developing into vesicles, containing a clear, watery, but afterwards straw-coloured lymph. These vesicles do not become pustular, as a rule, and are not attended by an inflammatory areola. They appear first on the trunk, especially the chest, then on the face and scalp, and finally on the limbs. They increase in size up to the third or fourth day, when they are as large as split peas. They become acuminated or conoidal, and finally burst, shrivel, and dry up. When air obtains access to the vesicles, the term windpox (*Varicella ventosa, emphysematosa*) is applied to the case. The visible mucous membranes, as well as the skin, are the seat of an eruption of flat vesicles, with lactescent contents. Umbilication is inconstant, often absent.

The febrile movement is not acute. It is remittent, increasing at night and in proportion to the amount of the rash, which may continue to come out in successive crops for as many as ten or twelve days. In very mild cases, fever may be entirely absent. Defervescence, when it occurs, takes place quickly.

The stage or process of desiccation varies in duration like that of eruption. Individual vesicles dry up quickly, their contents being in part absorbed, in part extravasated through bursting of their walls. A small brown crust

forms. When it falls off, "there remains only rarely a slightly depressed, smooth, soft, non-pigmented scar," which finally leaves no trace. A permanent pit, or scar, may remain when a vesicle has become a pustule. *Varicella bullosa* is due to a secondary infection with pyogenic micro-organisms. Unless in rare cases, there is no secondary fever, and chicken-pox, if uncomplicated, seldom or never destroys life. So-called relapses are probably examples of recurrent crops of the rash.

Complications and sequelæ may almost be said not to exist. Jonathan Hutchinson, however, drew attention to a formidable, though happily rare, variety of the disease, to which he gave the name of *Varicella gangrœnosa.* This dangerous form was described by Whitley Stokes, under the name of *Pemphigus gangrœnosus*, and was well known in Ireland in past times as "White Blisters," the "Eating Hive," and the "Burnt Holes." Radcliffe Crocker points out that this gangrenous eruption may occur in parts not the seat of the varicellous rash, and it is well known and is described as *Dermatitis gangrœnosa* by many writers. Varicella of the larynx is danger-ous, and may destroy life.

Diagnosis.—Chickenpox may be confounded with lichen, herpes, pemphigus, and varioloid. From the three first-named skin affections it is sufficiently distinguished by the age of the patients, their previous history, and the course of the disease. It is of the first importance to correctly diagnose varicella from smallpox. In cases of doubt it will be better for the physician to act as if the disease were really varioloid, in order to protect the community. At the same time, that varicella is a disease of its own kind absolutely distinct from smallpox, admits of no doubt.

Differential Diagnosis.—The grounds upon which a differential diagnosis is based are—

Chickenpox may prevail in an epidemic form without smallpox. On the other hand, varioloid has never been prevalent without coincident smallpox.

Young children are attacked by chickenpox, adults by smallpox, in a population protected by vaccination.

Varioloid was rare in prevaccination times, when chickenpox was as prevalent as it is now.

Vaccinated children readily take chickenpox—not so smallpox.

Children who have had chickenpox may, conversely, contract smallpox, even soon afterwards.

The two diseases may co-exist.

The virus of chickenpox never gives rise to smallpox, and the converse is believed to be equally true.

Smallpox is notoriously inoculable—not so chickenpox.

Smallpox rarely attacks the same person twice. Second attacks of chickenpox are not so uncommon.

The rash of chickenpox may set in after twenty-four hours—that of varioloid is postponed to the fourth or fifth day.

The febrile movement in chickenpox continues after the spots appear, —that in varioloid subsides.

In chickenpox, the spots come out in successive crops, and the fever is slight and remittent.

The characters of the spots are different in the two diseases.

Chickenpox is not a fatal malady, whereas even a mild form of smallpox may cause death.

Prognosis and treatment.—The simplest measures suffice in the

management of a disease which is generally so harmless. All that is necessary is to keep the child indoors, prescribe a milk and broth diet, avoid strong animal foods, and regulate the bowels by gentle aperients. If the skin is dry and itchy, it is most desirable to protect the vesicles from injury by rubbing or scratching, lest a secondary and more severe dermatitis, resulting in scarring, should be set up. In varicella of the larynx, either intubation or tracheotomy may be required.

<div align="right">J. W. MOORE.</div>

MORBILLI—MEASLES—RUBEOLA.

Syn., Fr., *Rougeole*; Ger., *Masern.*

A HIGHLY infectious, acute, febrile disorder, usually setting in with, and throughout accompanied by, catarrh of the mucous membranes, especially those of the eyes, nose, and respiratory passages; characterised by the appearance on the fourth day of a deep rose-red, or crimson inclining to purple, eruption of soft papules or pimples, which spreads over the whole body in the course of thirty-six hours, and is preceded and accompanied by sharp fever. This terminates by crisis between the sixth and eighth days, coincidently with the fading of the rash. Convalescence is apt to be complicated with affections of the glandular system and respiratory organs.

History.—The native seat of measles is unknown. The disease was probably widely diffused over Europe and Asia in the Middle Ages. Its distribution at the present day is practically coextensive with the habitable globe. Its separate identity was first shadowed forth by Forestus (1563), but it is to Sydenham (1676) that we owe the full differential diagnosis between measles and smallpox.

Etiology.—Measles is a disease of all ages, although children under 6 months enjoy comparative immunity, being less susceptible to the infection. In communities unprotected by a previous outbreak, measles attacks individuals of all ages. Striking illustrations of this statement are to be found in the history of outbreaks in the Faroe Islands (1846), the Fiji Islands (1875), and the Samoan group (1893). In all these instances age afforded no protection—old men and women falling victims as readily as young children, because they were not protected—had not been rendered immune—by a previous attack. Under these circumstances measles is a deadly disease.

The bacteriology of measles is as yet undetermined. In 1892, Canon and Pielicke described bacilli, which they found in the blood, expectoration, and nasal and conjunctival mucus of patients suffering from measles, and which they believe to be specific. In any event, the *materies morbi* may be held to exist in the expectoration, the mucous discharges, and the cutaneous *débris*. Measles is infectious, from the first sneeze or cough. Hence the difficulty of controlling its spread. It is most infectious, however, in the eruptive stage, and probably not very infectious in desquamation. Its "striking distance" is believed to be considerable, but the contagium is less persistent than that of scarlatina. One attack usually, but not necessarily, protects from a second—acquired immunity is not so constant after measles as it is after smallpox. The disease may attack the *fœtus in utero*. Measles prevails chiefly in the spring and autumn. A mean temperature

above 58°·6 and one below 42° are equally inimical to its prevalence. These facts are well illustrated in Fig. 17, which shows the seasonal prevalence of measles in London during fifty years, 1841–1890, as proved by the returns of the registrar-general for England.

Morbid anatomy and pathology.—A specific catarrhal inflammation of the mucous membranes of the respiratory and of the intestinal tracts is first among the pathological changes in measles. The nasal mucus, according to Mayr and Hebra, is at first transparent, afterwards opaque; its reaction is always alkaline.

G. Simon ascribes the measles papule to œdema of the cutis, not to exudation in the hair follicles and sebaceous glands. In this view Unna coincides. He holds that the appearances point to the fact that spastic resistance in the cutaneous vessels is added to the primary congestive hyperæmia, which develops around the infection in the capillaries. Œdema of the cutis and the hypoderm exists, whereas there is an almost complete absence of a cellular exudation. In 1891, Catrin examined a case of *rougeole boutonneuse*, or "nodular measles," and found in the papule
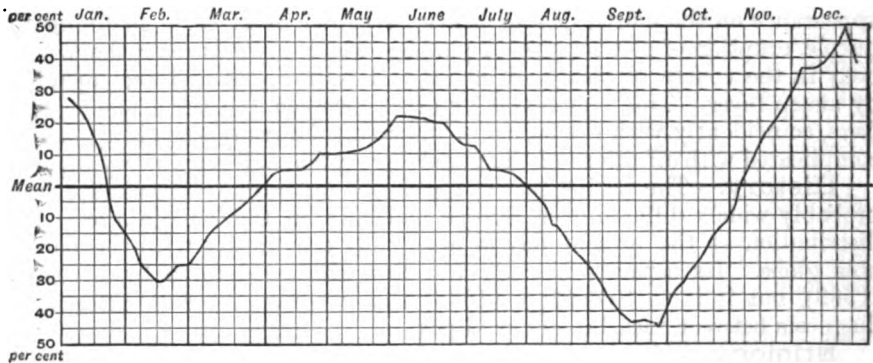
FIG. 17.—Measles mortality curve.

marked diapedesis of white corpuscles, especially along the blood vessels, follicles, and coil glands. He further described, as characteristic of the nodular form of the eruption, a series of deep epithelial changes, consisting of colloid transformation and coagulation necrosis of the epithelium. Unna thinks that we should regard these changes as a direct result of the specific poison, which has somehow exceptionally reached the epithelium, as it does in smallpox. The scaling of the epidermis in these severe cases is naturally more profound and persistent.

Symptomatology.—**Stages.**—A typical case of measles runs through four stages—incubation, invasion, eruption, and desquamation.

Incubation.—Ten days as a rule elapse between the reception of the poison into the system and the development of the earliest febrile and catarrhal symptoms. This stage is shortened to eight days after inoculation. Few or no symptoms attend this preliminary period. Towards its close, fatigue, lassitude, and nausea may be felt, and there is sometimes an ephemeral or passing·fever, followed by defervescence.

Invasion.—The initial or prodromal stage is longer in measles than in any other of the exanthemata. It lasts four or five days. The attack begins suddenly with the ordinary nervous symptoms of an acute fever, and in addition a remarkable group of symptoms connected with the

mucous membranes—sneezing, itching, and swelling of the eyelids, which are intensely red on the inside; watering of the eyes, which look bloodshot and shun the light. The nose feels stuffed and often bleeds; the patient has a "bad cold in the head." The throat is raw and sore, the voice becomes husky, and a hoarse, brassy cough sets in, occurring in paroxysms. In many cases there is a catarrhal diarrhœa, the motions being green and unhealthy in appearance and odour. On the second day an accidental erythematous rash may show itself, simulating scarlatina. The skin is hot and dry, and the thermometer rises to 102°·5 or even 104° F. by the evening of the first day. This initial fever gives way quickly, so that on the morning of the third day the temperature is normal (98°·4 F.), or only slightly febrile (99° or 100° F.) As the true rash appears, the temperature again rises briskly. Even on the second day an eruption of scattered points and spots may be seen on the soft palate and buccal mucous membrane. Koplik has recently drawn special attention to these spots. Drowsiness and sleepiness are constant symptoms in the pre-eruptive stage.

Eruption.—Towards the close of the fourth day, the true rash is heralded by a renewed rise of temperature and an exacerbation of all the symptoms connected with the mucous membranes. The eruption shows on the face first, next on the back of the wrists, afterwards on the trunk, lastly on the limbs. It consists of small red specks, slightly elevated and velvety to the touch, on the forehead and face closely resembling flea-bites. These specks become grouped in crescentic patches, leaving interstices of skin of normal colour. The rash, therefore, is in general discrete rather than confluent. It is of a deep rose or crimson hue, inclining to purple. The face swells somewhat. Miliary vesicles with an inflamed red base may appear in crops. The rash sometimes turns livid or black. The perspiration has a peculiar heavy odour, compared by Niemeyer to the smell of a freshly plucked goose.

The rash develops fully in thirty-six hours. It is then dusky, while the skin looks rough and dirty—it is beginning to peel or desquamate. As the rash comes out the coryzal and catarrhal symptoms increase, and so does the fever to 104° or 105° F.—being most intense when the eruption is at its height on the evening of the fifth day, or on the sixth day.

With the fading of the rash defervescence begins, and is almost completed within forty-eight hours, being so rapid and sudden as to be diagnostic. As the rash fades it leaves yellowish red stains, which may persist for several days, resembling the *measly* rash of typhus fever. The morbillous catarrh—both respiratory and intestinal—frequently persists at this stage, and a nummular sputum shows that the bronchioles share in the affection.

Desquamation.—This commonly begins about the eighth and ends about the eighteenth day. The skin peels off in fine, branny scales, hence the term *furfuraceous* desquamation. This may escape notice, but a careful search will reveal it across the bridge and along the sides of the nose, as well as about the mouth and on the neck.

In uncomplicated measles convalescence is complete in eighteen days from the earliest symptoms. In rare cases a relapse of the true rash has been known to occur, together with a return of the fever movement. These relapses are of short duration.

According to Thomas, measles in which there is rash but no catarrh is especially apt to occur in very young infants, and is attended with little or no fever. Probably many cases of Rötheln (rubella) were formerly

classified as non-catarrhal measles. The occurrence of measles without the rash is probably a rare clinical experience.

Of malignant measles, three varieties are named—Purpuric measles ; asthenic or adynamic measles ; and complicated measles.

The purpuric variety is very infrequent. It is observed chiefly in young and sickly children. The rash is profuse and dark, the skin is dotted over with petechiæ and vibices, while blood oozes from the several mucous membranes. In the asthenic or adynamic form the symptoms are severe and persistent—the fever runs high, causing early exhaustion, the pulse becomes rapid and weak, delirium gives place to somnolence, and the patient sinks into the typhoid or ataxic state. This term is applied to a group of symptoms which indicate extreme nervous prostration, namely, sleeplessness, low muttering delirium, small rapid pulse, quick shallow breathing, agitation and restlessness, tremors, plucking at the bedclothes, dilatation
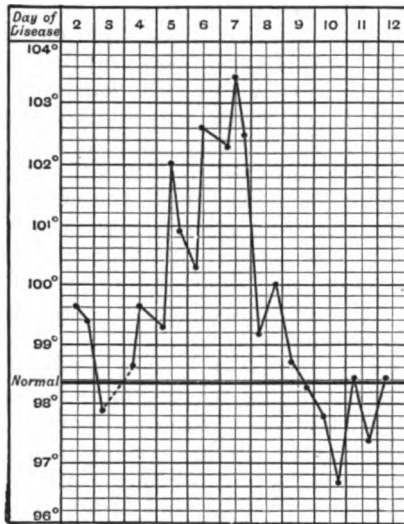
FIG. 18.—Ordinary Measles.
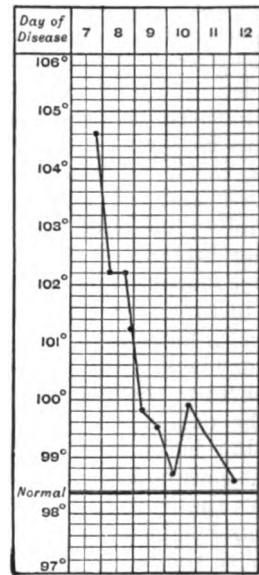
FIG. 19.—Defervescence in Measles.

of the pupils, and in the end deepening coma, or unconsciousness and insensibility.

Complications.—The chief complications of measles are—convulsions in young or nervous children, spasmodic catarrhal laryngitis, suffocative catarrh, diarrhœa, colitis, with glairy, bloody, offensive stools, and tenesmus; epistaxis or nose-bleeding, otitis, diphtheria of the pharynx and larynx (membranous laryngitis or true croup), capillary bronchitis and catarrhal pneumonia, pleuritis, and, in the stage of desquamation, glandular enlargements in the neck and thorax, cancrum oris or noma, gangrene of the vulva, acute miliary tuberculosis, and chronic ophthalmia, with granular lids.

Suffocative catarrh may occur in any stage of measles. Its symptoms are—high fever, oppression of the chest, dyspnœa, and moist cough. In young children this disseminated broncho-pneumonia (for such it is) is dangerous from purely mechanical causes—suffocation is brought about by œdema of the bronchial mucous membrane, paralysis of the muscular fibres

of the bronchioles, and resulting accumulation of secretion. An attack of measles, besides giving rise to complications and sequelæ such as have just been named, often sows the seed of even a fatal constitutional delicacy.

Temperature.—The fever movements in measles are highly characteristic. In the stage of incubation, a short preliminary fever in the form of an *ephemera* may occur—the thermometer possibly rising to 102°·8 or 103°·6 F. An initial or prodromal fever constantly occurs in the stage of invasion, temperature rising to 102°·4 or even 104° F., on the evening of the first day. A fall succeeds, temperature being either normal or subfebrile on the third day. The true eruptive fever begins shortly before the rash is due, develops with the out-coming of the rash, and reaches its height in some thirty-six hours. It lasts from one and a half to two and a half days, and gives way by a rapid defervescence or crisis, except where a complication exists. These changes are well shown in Fig. 18. The central defervescence in measles is illustrated in Fig. 19. Figs. 20 and 21 are interesting, as showing the exact duration of incubation in measles.

Diagnosis.—The recognition of measles depends, first, on the exanthem or rash; secondly, upon the mucous membrane symptoms, and the characters of the fever (the behaviour of the temperature); thirdly, upon a consideration of the existing epidemic and the exposure of the patient to the virus of measles.

The disease may be confounded with Rötheln (rubella), scarlet fever, variola, varicella, simple roseolar rashes, and typhus fever.

The most common error of diagnosis is between measles and smallpox, but the development of the pustular rash of the latter sets the question at rest. At the beginning, also, confluent smallpox presents an eruption on the second day, compared with the fourth or fifth day in measles. The papules of smallpox are hard and shotty; those of measles are soft and velvety. The following method, called the "Grisolle sign," is a certain means of diagnosis. If upon stretching an affected portion of the skin the papule becomes impalpable, the eruption is caused by measles; if, on the contrary, the papule is still felt when the skin is drawn out, the eruption is the result of smallpox.

Prognosis.—This, in primary and uncomplicated measles, is thoroughly favourable. The mortality varies greatly. Sometimes only 2 or 3 per cent. of the patients die; occasionally the death rate reaches the alarming figure of 50 per cent. Measles is mild in sucklings under 6 months old; it becomes severe at the first dentition, and is sometimes very severe in adults. In pregnancy it is dangerous. It is most fatal among the ill-nourished, rachitic, or tuberculous denizens of a large city.

Unfavourable symptoms are great weakness and excitement from the outset; a hot, dry skin; a hard and rapid pulse; quick, laboured respiration, with a short cough; early fading of the rash. By far the most fatal complication of measles is bronchitis in its severer forms.

Treatment.—Little can be done to prevent the spread of measles, because it is infectious from the start, while the first case in a household may be mistaken for a severe feverish cold. When a person has been exposed to the infection, he cannot be pronounced safe within sixteen days at least. A convalescent from measles should not be declared free from infection until three or preferably four weeks have elapsed from the first symptoms.

As regards curative treatment, Hilton Fagge aptly points out that " the general plan of treatment in measles and in scarlatina is the same,
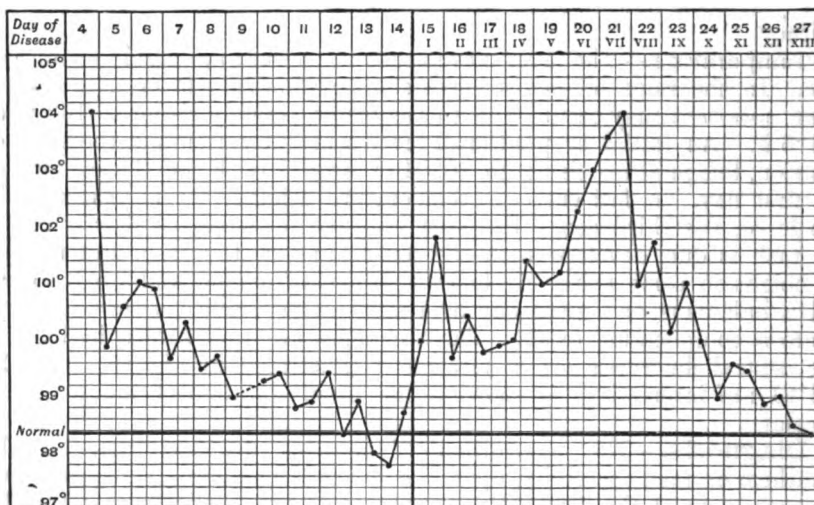
FIG. 20.—Measles after scarlatina.

for in neither of these maladies have we any specific method of dealing with the malady itself." A mild equable atmosphere is essential (60° to 65° F.). The steam-kettle should be used in winter. Ventilation should
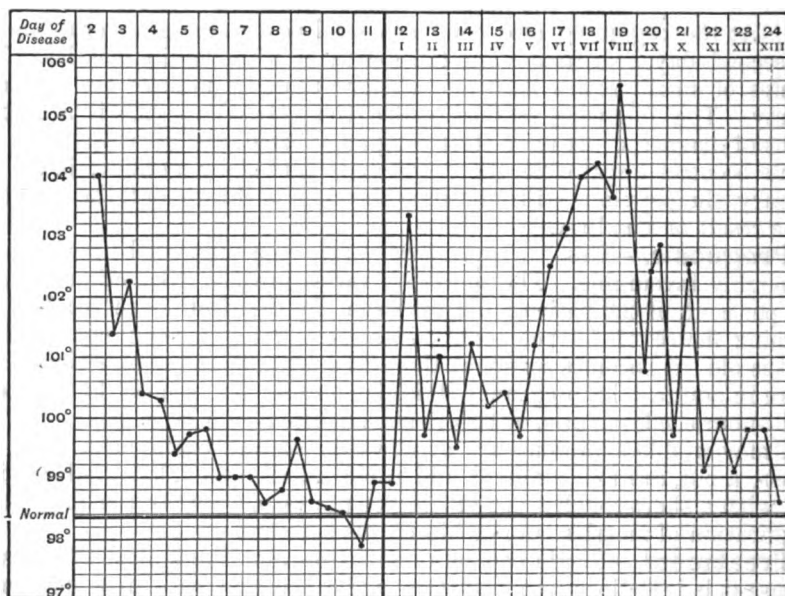
FIG. 21.—Measles after scarlatina.

be draughtless. Children must be watched at night, lest they should throw off their bed-clothes. The hands and face may be washed daily, and the whole surface may be cautiously sponged and afterwards oiled—

liniment of camphor, a weak carbolised oil or soft paraffin, or hazeline cream being used for the purpose. Shelly reports unfavourably on eucalyptus inunction. All exposure to cold must be carefully avoided until catarrhal symptoms have passed away. In convalescence, fresh air, driving in the open country, and change of air to the seaside, or some sheltered inland health resort, are desirable. Among drugs suitable for convalescents from measles are quinine, saccharated carbonate of iron, cod-liver oil with saccharated solution of lime, chloride of calcium, and syrup of the lactophosphate of calcium. The skill of the physician is often taxed to the uttermost in the treatment of the complications of measles.

In malignant measles, Dieulafoy recommends a bath at 26° C. (78°·8 F.) for twelve minutes, with cold affusion to the head. The cold bath re-establishes the secretion of urine, the skin becomes soft, and temperature falls.

In initial convulsions Trousseau's advice is excellent—"Wait, avoid boisterous practice." A warm bath may be given, or compression of the carotids may be practised, in the way recommended by Trousseau, the common carotid artery on the side of the neck, opposite to the side convulsed, being pressed upon for some minutes at a time.

In false and true croup, the patient should be placed in a croup tent, and for twenty or twenty-five minutes relays of sponges soaked in hot water may be applied to the neck and throat. In suffocative catarrh, hot poulticing does good, and the chest may be wrapped in cotton-wool or French wadding, after rubbing with chloroform and ammoniated camphor liniment. Inhalations of oxygen should be tried.

Diarrhœa is often checked by good nursing and suitable dieting. A teaspoonful dose of a mixture composed of five drops each of glycerin of carbolic acid and tincture of chloroform and morphine in cinnamon water may be given occasionally, except to a very young child. If colitis occurs, albuminous enemata are of use.

Ophthalmia and glandular enlargements require constitutional treat-ment—a generous, wholesome dietary, with milk, eggs, cod-liver oil, and such drugs as iron and quinine, iodide of iron, chloride of calcium, and arsenic.

Should stimulants be required, white-wine whey, brandy and warm milk, or egg-flip will be most suitable for children.

J. W. MOORE.

SCARLATINA—SCARLET FEVER.

Syn., Lat., *Febris Rubra;* Fr., *Fièvre rouge—Scarlatine;* Ger., *Scharlachfieber,* or shortly, *Scharlach.*

An acute, specific, infectious fever, characterised by a sudden onset, with vomiting, rigors, and prostration; early and persistent sore-throat, deep injection of the mucous membranes of the throat, which are swollen and inflamed, very rapid pulse rate, and high fever; and especially by the appearance on the skin after a few hours of a minutely punctiform scarlet rash, which is most intense on the third day, and afterwards fades gradually, to be succeeded by profuse desquamation of the cuticle

in both small and large flakes. A specific nephritis is a not uncommon complication or sequela. Three varieties of the disease are recognised, namely, simple, anginose, and malignant scarlatina.

History.—The origin and native habitat of scarlet fever are unknown. It is most widely distributed on European soil, especially in the north-western and northern countries. Its diffusion in Africa and Asia is limited. It is rare in India, unknown in Japan. In 1848 it broke out in Australasia, where it generally assumes a mild type. Its first outbreak on
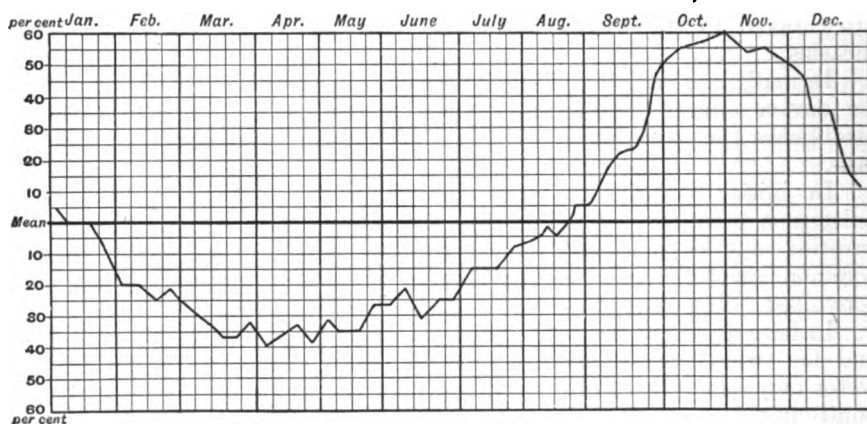
Fig. 22.—Scarlatina mortality curve.

North American soil took place in 1735, when it broke out in Kingston, Massachusetts, and overran the New England States within a few years. Not until 1830 did it become diffused over South America.
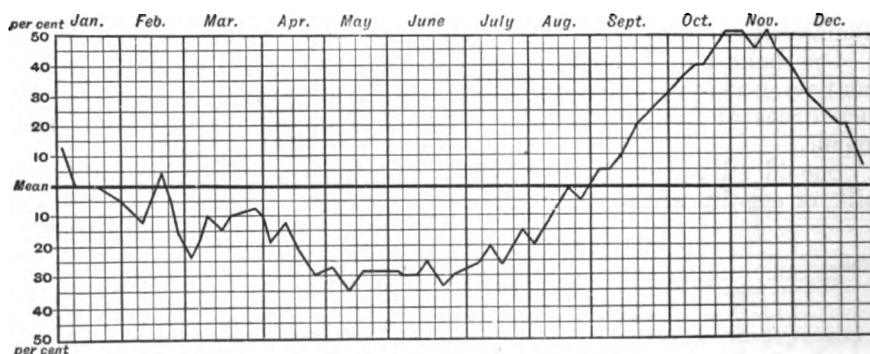
Fig. 23.—Enteric fever mortality curve.

The area of prevalence of scarlet fever is much smaller than that of smallpox or of measles. Its epidemics arise at long intervals of ten, or even twenty, years. It shows extreme variation in severity—the death-rate being almost nil, or only from 3 to 5 per cent., in some outbreaks, but rising to 30 per cent. or more in others—so widely does the epidemic constitution vary.

Etiology.—Climate does not play a prominent part as a predispos-ing cause, while season does. Scarlatina tends to increase during the second half of the year, attaining its maximal prevalence in the fourth

quarter. When the mean temperature rises much above 50° F., scarlatina spreads; a fall of mean temperature below this critical point in autumn checks its prevalence. Diphtheria and typhoid fever obey the same law of seasonal prevalence. The facts relating to scarlatina and enteric fever are shown in Figs. 22 and 23, based on returns of the registrar-general for England for a long series of years. The curves refer to deaths in London. The close accordance in the two diagrams is very remarkable. Traumatism is a predisposing cause, the disease being conveyed through the infection of a wound, the result of injury or operation. Such is the so-called surgical scarlatina. Sometimes this form of scarlatina is spurious and septicæmic in origin. More females than males are attacked. Age is a potent predisposing cause, for the disease is essentially one of childhood and adolescence. Goodall and Washbourn give the following table, which shows the number of admissions and deaths at various ages in the hospitals of the Metropolitan Asylums Board, London, from 1871 to 1894, together with the percentage fatality :—

Ages.	Cases Admitted.	Deaths.	Fatality per Cent.
Under 5 years	23,072	4,052	17·6
5 to 10 ,, ...	33,647	1,789	5·3
10 ,, 15 ,, ...	14,399	345	2·4
15 ,, 20 ,, ...	5,319	139	2·6
20 ,, 25 ,, ...	2,509	65	2·6
25 ,, 30 ,, ...	1,215	38	3·1
30 ,, 35 ,, ...	665	31	4·7
35 ,, 40 ,, ...	281	16	5·7
40 and upwards . . .	243	15	6·2
Total	81,350	6,490	8·0

The specific character of the poison of scarlet fever is unquestionable. The *contagium vivum* is singularly retentive of life, and is most active. The virus may be conveyed by fomites, such as articles of dress, bedding, carpets, furniture, and even letters. It may also be inhaled, swallowed in water or milk, or carried by means of domestic animals, such as dogs and cats. Scarlatina may be inoculated by means of the blood, the epidermic scales, and the serum from cutaneous vesicles. The urine also is believed to be infective.

Klein cultivated a streptococcus from the blood of patients during the acute febrile stage of scarlatina. The same streptococcus was found in connection with an eruptive (ulcerative) disease on the teats and udders of milch cows, at Hendon, in 1886. To the consumption of the milk from these cows an extensive outbreak of scarlet fever in the north of London was definitely traced by Power. This micro-organism—the *Streptococcus scarlatinæ*—grows slowly on gelatin, in opaque white colonies, and does not liquefy the gelatin. When grown in milk, it coagulates or curdles it. Cultivated in broth, it forms long and exquisite chains. This microbe apparently conforms to Koch's law, and is therefore regarded as specific by Klein. Thus it may be found in many cases of scarlatina; it can be cultivated outside the human body in suitable media, as above—gelatin, milk, broth; and its pure cultures possess the power of setting up a disease in animals, resembling scarlatina.

Sternberg, however, considers that the specific infective agent in scarlet fever has not been demonstrated. In the secondary affections, attended by suppuration, one or other of the common pyogenic micrococci is usually found, and is doubtless the cause of the local inflammatory process. Crajkowski (1895) found a diplococcus present in comparatively small numbers in the blood of fifteen scarlatina patients. He does not, however, claim for this diplococcus a specific character.

Morbid anatomy and pathology.—The blood is darkened in colour, thin, and generally contains an excess of white blood corpuscles.

The cutis of the scarlet fever skin is, according to Unna, characterised by an enormous paralytic dilatation of the blood vessels. The capillaries of the papillary body, as well as of the cutis proper, are all distended, as if by a forcible arterial injection; the cutaneous vessels, from the lower cutis margin onwards, are almost all of equal calibre. The fact that this great dilatation of vessels is found everywhere, even on pieces taken from the cadaver, points to a maximal vascular paralysis at the height of scarlet fever. All signs of marked cutaneous œdema are absent, although the scarlet fever skin is "puffy," owing mainly to the overfilling of its vessels with blood. In the epidermis we find, even at the height of the rash, an abnormal development of its horny layer; this, later on, in different ways, leads to scaling, while the prickle layer shows neither œdema nor emigration of white blood corpuscles. The process of desquamation may involve the nails of the fingers and toes, and the hair may fall out. Warts have been known to drop off after scarlet fever. Unna holds that the epidermic changes are much more easily explained as direct specific actions of the poison than as the hurtful results of a simple dermatitis.

In the intestines the appearance known as *psorenterie* is caused by swelling and prominence of Brunner's and Lieberkühn's glands, as well as of the solitary follicles and Peyer's patches. In the kidneys a catarrhal condition is found early in the disease; a true parenchymatous nephritis sets in later. In a still more advanced stage, an interstitial nephritis may supervene. The heart muscle suffers severely. Its fibres are the seat of an acute molecular disintegration, to which have been given the various names of acute parenchymatous myocarditis, acute parenchymatous degeneration, albuminous degeneration, febrile softening of the heart, infectious myocarditis. The change may be the result of the specific action of the fever poison, or of the pyrexia, or of both, on the protoplasm. There is a conflict of opinion as to whether the condition is inflammatory, or merely degenerative. As regards the symptoms, cardiac failure is the chief evidence of this condition of the endocardium.

Symptomatology.—Cases of scarlatina are arranged under three headings—

Scarlatina simplex, or mild scarlet fever, in which the disease runs its course without complications or untoward sequelæ, terminating in an uninterrupted convalescence.

Scarlatina anginosa, in which the affection of the throat is severe, and the cervical glands are sharply engaged.

Scarlatina maligna, in which extreme nervous prostration, with its attendant "ataxic" or "typhoid" symptoms, is the most striking and ominous phenomenon.

Incubation.—This period is very short, probably never exceeding a week, and rarely lasting so long. It may be only twenty-four hours, but

on the average it varies from three to five days. Consequently, a person who has been exposed to the poison of scarlatina, and does not sicken after a week's quarantine, may be pronounced safe. This stage of latency may be unattended by symptoms, or towards its close there may be slight headache, malaise, lassitude, and loss of appetite.

Invasion.—This pre-eruptive, prodromal, or initial stage is shorter in scarlatina than in any other fever. It is most commonly only twenty-four hours in duration. The onset is abrupt. In children, the earliest symptoms are usually vomiting, diarrhœa, rigors, or a convulsion—the last named a sign of danger. In adults, sore throat ushers in the attack. It is accompanied by chilliness or rigors, headache, malaise, and prostration. Pulse and temperature rise quickly. The rapidity of the pulse—140 to 160 beats a minute—is almost pathognomonic of scarlatina. The skin is hot and dry, the pungent heat being like that of acute pneumonia. The tonsils, soft palate, and uvula are deeply injected, plum-coloured, and swollen. The cervical and submaxillary glands also are usually engaged, but the Schneiderian mucous membrane and conjunctivæ generally escape.

Eruption.—The rash may be detected very early on the sides of the neck and over the chest, and near the larger joints. It afterwards spreads to parts of the face, the abdomen, and the limbs. The centre of the chin and a zone round the mouth, as well as the scalp, usually remain free from the rash. So also do the palms of the hands and soles of the feet. The eruption consists of minute red dots, with surrounding paler halos, which run together, causing a general or patchy suffusion of the skin of a bright scarlet colour, which suggested to Sir Thomas Watson, a comparison to a boiled lobster. The eyelids, cheeks, hands, and feet commonly swell slightly. The contractile power of the cutaneous arterioles being increased, on pressure a white stripe or streak develops, and lasts for a few moments. This is the so-called *Tache scarlatinale*, a diagnostic sign of some value.

Sometimes a millet-seed rash of tiny vesicles is observed. These become filled with a milky fluid after thirty-six to forty-eight hours. In other cases the rash is blotchy, macular, or papular. In complicated or malignant cases the rash is badly developed, or fails to appear. After two or three days the eruption fades slowly, leaving persistent petechial lines in the folds in front of the elbows, in the armpits, groins, and popliteal spaces. These streaks may help in diagnosis. The fever runs high in the eruptive stage, and the pulse beats fast. The tongue is at first coated with a thick, creamy, white fur, through which the enlarged papillæ project as little scarlet protuberances. The fur is shed quickly, leaving the tongue red and raw, resembling a ripe strawberry. Hence the expressions strawberry tongue, and cat's tongue. Defervescence is gradual, by lysis, extending over from two to eight days. The temperature spikes somewhat—rising in the evenings, falling in the mornings.

Desquamation.—The process called "peeling" sets in on the neck and chest, between the sixth and ninth days. Then it affects the limbs, hands, and soles of the feet. Branny scales come off from the face, flakes of dead cuticle from the trunk, and sometimes gloves of skin from the hands and feet—even the nails may occasionally be shed. Wilks drew special attention to an atrophic transverse furrow or groove in the nails of scarlet fever patients. On the body, desquamation begins by an elevation of the horny layer of the epidermis into little circular mounds.

The tops of these are rubbed off or split, leaving ring-shaped free edges. The rings spread outwards, and coalesce with each other.

In this stage, albuminuria often makes its appearance, one reason being
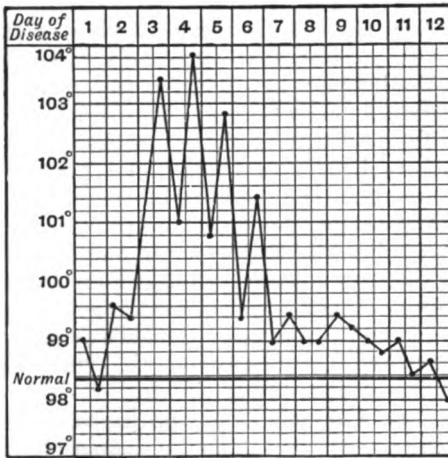
FIG. 24.—Simple scarlatina.
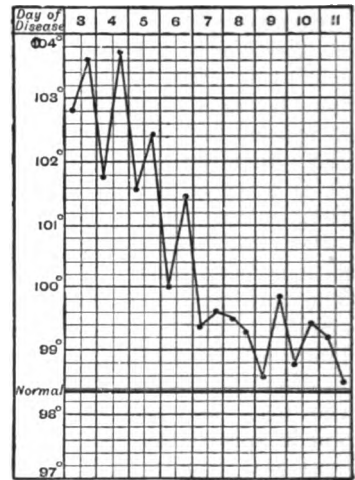
FIG. 25.—Simple scarlatina.

the shedding of the dead tubal epithelium in the kidneys, in consequence of which albumin escapes into the urine. The duration of desquamation is indefinite—in some cases it lasts for a fortnight only; in others, for several weeks, perhaps for months.

Relapse is a very infrequent occurrence, but undoubted examples are from time to time recorded. It may be caused by auto-infection, or by re-infection through a prolonged sojourn in scarlatina wards.

Irregular or aberrant forms of scarlatina often present themselves. Of the rudimentary or abortive and therefore mild forms, the most frequent is simple scarlatinal angina, or sore throat. We also meet disguised or latent scarlet fever—the form to which Trousseau gave the name of *Scarlatine fruste.*

FIG. 26.—Anginose scarlatina.

In marked contrast to these mild forms, we often come across that severe variety called *Scarlatina anginosa.* Pain and stiffness about the jaws are early symptoms. The throat feels raw, deglutition is difficult and painful, there is hoarseness, the tonsils are swollen, of a deep purple hue, and coated with small, whitish specks of exudation. Offensive

sanious discharges take place from the nostrils, irritating the neighbouring skin, the breath is fœtid, the voice becomes nasal, liquids return by the nostrils, and deafness may occur, owing to extension of the disease through
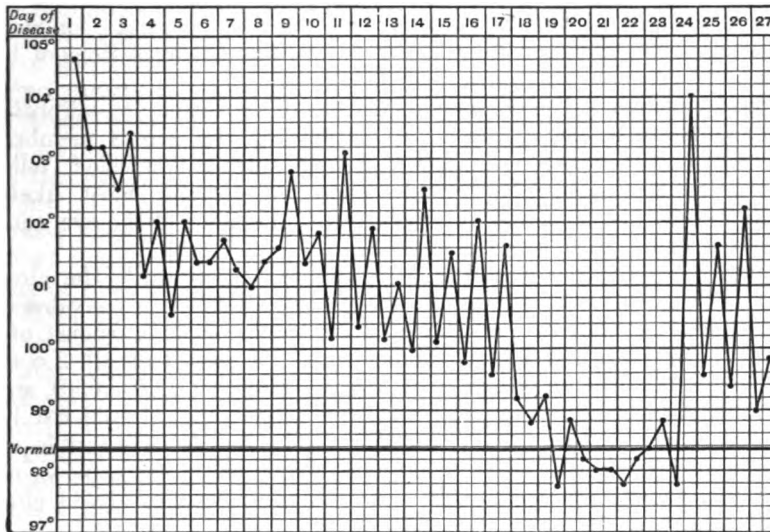
FIG. 27.—Ataxic scarlatina.

the Eustachian tubes. The cervical glands swell enormously, and diffuse cellulitis of the neck may cause the very fatal condition known as " tippet neck." Diphtheria is a not uncommon complication in this form of scarlatina. The tonsils and soft palate may undergo necrosis in patches and slough away.

The term *Scarlatina maligna* is reserved for two terrible varieties of the malady, namely, ataxic scarlatina and hæmorrhagic scarlatina. They constitute the *Scharlachtyphus* of Hebra.

Nervous or ataxic scarlet fever is ushered in with rigors, convulsions, and even tonic spasms, with trismus, incessant vomiting, and diarrhœa, wakefulness, agitation, and restlessness with delirium, and hyperpyrexia—110°·3 F. (43°·5 C.) was observed by Wunderlich. Ataxic symptoms quickly follow—muscular tremors, plucking at the bedclothes, the *coma vigil* described by Jenner, dilated pupils, coma, quick shallow breathing, extreme feebleness of the heart's action, and profuse cold or clammy sweating. In these cases the rash is badly developed, and life ebbs quickly.

FIG. 28.—Malignant scarlatina.

In the very rare form known as hæmorrhagic scarlatina, the rash
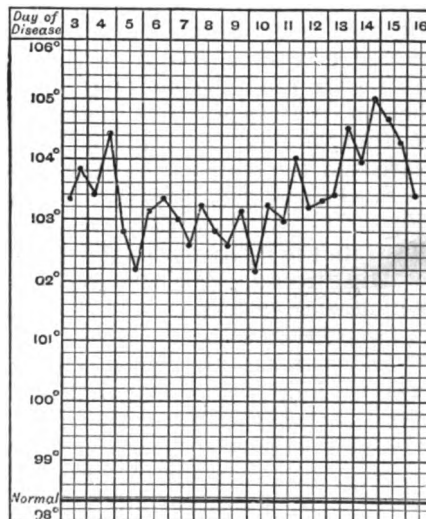
comes out late and imperfectly. Its colour is dark, and reddish brown points of hæmorrhage, with petechiæ and vibices, are found scattered over the surface in children, less extensively in adults. The tonsils and gums are dark-coloured, and hæmorrhages take place from the mucous membranes, especially of the nose, colon, and urinary organs. In women, menorrhagia may occur. Pleuritic or pericardial extravasations of blood may take place.

Complications.—The chief complications of scarlatina are—diphtheria, acute rheumatic arthritis, and inflammations of the serous membranes, acute desquamative nephritis, pleuritis with purulent effusion, bubonic swellings in the neck. In convalescence, the sequelæ most likely to occur are—pyæmia, boils and abscesses, otitis, affections of the eye, eczema, and chorea, or St. Vitus's dance.

Acute desquamative nephritis generally sets in towards the close of the first week. It may appear in the second week, or in convalescence. It is ushered in with suppression of urine, or hæmaturia, œdema of the eyelids, pallor, thirst, and high temperature. If passed at all, the urine is scanty, highly albuminous, of high specific gravity (1020–1030), smoky appearance, and acid reaction. Under the microscope, altered red blood corpuscles, and granular, bloody, and epithelial tube casts are visible. The affection may terminate in recovery (the urine becoming copious, clear, and of low density), in death with convulsions, or, very rarely, in chronic general nephritis.

Temperature.—The behaviour of the temperature in scarlatina is less typical than it is in smallpox or measles. At the outset it rises rapidly and continuously in a few hours to 103° or 104° F. With the coming out of the rash a further rise is observed to 105°, but seldom in cases which end favourably to 105°·8 or upwards. As a rule, the intensity of the fever bears a tolerably close relation to that of the rash. With the fading of the rash defervescence begins. It may be sudden, but generally it is protracted, extending over from three to eight days. The evening readings are higher than the morning ones. Complications of course modify the temperature range. The thermometer may fall below normal at the end of defervescence, and other collapse symptoms may appear. In typhoid-scarlatina the temperature may present a subcontinuous or remittent type. In fatal cases hyperpyrexia is common. The series of temperature charts (Figs. 24–28), from cases under my own observation, is intended to illustrate the behaviour of the temperature in scarlatina of varying types.

Diagnosis.—We have to distinguish scarlatina from erythema, smallpox, measles, epidemic rose rash or rubella, erysipelas, tonsillitis, diphtheria, and acute rheumatism.

In erythema the fever is slight; there is no sore throat, glandular swelling, kidney affection, or desquamation. Smallpox could only at the outset be mistaken for scarlatina. The adventitious prodromal rash, and a certain amount of sore throat, may cause confusion for a while. In measles the early angina, the strawberry tongue, and the glandular swellings of scarlatina are wanting, while the catarrhal symptoms are characteristic. The diagnosis between scarlatina and rubella is often difficult. In the latter disease the rash shows on the face; it fades soon, the fever is moderate, the pulse rate relatively slow, angina is trifling, and the occipital glands are large and hard. In acute tonsillitis, cynanche tonsillaris, or quinsy, one tonsil is generally more engaged than the other; vomiting, rash, and albuminuria are wanting. Diphtheria, seemingly

primary, may really be complicating scarlet fever, with a badly-developed rash. Note should be taken of any prevailing epidemic. Acute rheumatism usually attacks adolescents or adults. It is distinguished from scarlet fever by its symptoms and course, by its profuse acid and sour-smelling perspirations, and by the absence of the glandular swellings and renal complications of scarlatina.

Prognosis.—This is always uncertain, for scarlet fever is one of the most treacherous of maladies. Therefore, a guarded opinion should be given, no matter how mild the attack may seem to be. The rate of mortality frequently reaches 15 per cent. It may touch 25, 30, or even 40 per cent. It is influenced unfavourably by age, social status, family idiosyncrasy, pregnancy, and previous ill health. Among children under 5 years of age it is, on an average, nearly 20 per cent., or one in five, as may be seen in the table on p. 171. In a given case, unfavourable signs are—Hyperpyrexia, dyspnœa, extreme rapidity and feebleness of the pulse, early collapse, badly-developed and dark-coloured rashes; persistent vomiting and diarrhœa; delirium, or coma; sloughing of the fauces, diphtheria, purulent arthritis, and other severe complications, especially nephritis, with anuria and diffuse cellulitis of the neck.

Treatment.—The prophylaxis of scarlet fever is not attended by the vast difficulties which beset the attempt to control the spread of measles. Breathing time is allowed the physician in which to plan and give effect to precautionary measures, for there can be little doubt that the poisonous virus is shed in greatest quantity during the later stages of the disease, in the discharges from the nose and throat, in the motions from the bowels, in the urine, but, above all, in the peeling cuticle.

All known drugs are without avail as prophylactics, and we have not as yet discovered a specific remedy for scarlatina. The only effectual prophylaxis consists in isolating the patients from those who are unaffected as early and as completely as possible. The isolation or insulation of the sick should be kept up until desquamation has finally ceased. A scarlatina patient may go home or rejoin school, provided he and his clothes have been thoroughly disinfected, *in not less than six weeks from the appearance of the rash,* if desquamation has completely ceased, and there is no complaint or sign of sore throat, or of discharge from the nose or ears.

The term curative treatment must, in the absence of a specific for scarlatina, be taken in a qualified and restricted sense to express the measures we adopt to help the patient safely through his illness. The treatment must be largely symptomatic, and directed mainly against those complications and sequelæ which disturb the regular progress of the disease.

The sick-room should be fresh and airy. The bed-covering should be light. Very little furniture should be allowed. There should be no curtains or carpets. A daily toilet is a necessity, and tepid sponging of the whole body is useful and refreshing. Indeed, warm or tepid baths may be given from the outset, as a means of freeing the patient from infection.

The bed- and body-linen may be changed as often as required. The diet should consist of weak meat-broth, chicken-broth, gruel, milk (plain or renneted, or peptonised, or mixed with aërated water, or lime-water in varying quantity), oranges, and cooked fruits. Cool, refreshing drinks, such as cold spring water, lemonade, acidulated water, are to be given freely and at short intervals. The urine should be examined daily. The hot-air or vapour-bath may be used if albuminuria is present, and, during desquamation, the tepid bath will be found both grateful and beneficial.

It may be given daily, and followed by dry rubbing and inunction with weak carbolised oil (1 to 2 per cent.), or soft paraffin, or camphorated oil. Ten grains of thymol may be added to an ounce of soft paraffin, or simple ointment, as a disinfectant. Scarlatina is a great blood destroyer, and, in convalescence, iron will be required, as well as change of air to the mountains or the seaside.

In scarlatina anginosa, the cold-water treatment may be adopted to reduce hyperpyrexia. Cold baths, the wet pack, cold douches, the internal administration of large quantities of cold water, either by the mouth or by enema, all absorb a large amount of heat from the body, while they rather augment the formation of heat. Hence the patient is not depressed, and does not become collapsed. The constant swallowing of fragments of ice is grateful and effectual. Cold compresses of lint, moistened with water and glycerin, should be wrapped round the throat. The nostrils, mouth, and pharynx should be frequently washed or sprayed with a disinfectant, or antiseptic solution, such as sulphurous acid, chlorine water, permanganate or chlorate of potassium, or glycerin of carbolic acid. Caustics of all kinds, in my opinion, had best be avoided. Pain may be relieved by painting with a solution of cocaine. Quinine, ferric chloride, guaiacum, carbonate of guaiacol, salicylate of sodium, and tincture of acetate of iron with glycerin, are among the most useful drugs. Lastly, a moderate, sometimes a free, allowance of stimulants is necessary.

The treatment of scarlatina maligna is too often of no avail, the patient dying, poisoned, in a few days or even hours. Ataxic symptoms must be combated by the free administration of liquid food and stimulants, and by the exhibition of such remedies as carbonate of ammonia, quinine, bark, iron, camphor, and musk. Derivation to the surface may prove of use. It is carried out by wrapping the lower limbs and body in flannels or in cloths wrung out of mustard and hot water, or by the warm or hot bath; or by the cold pack and cold affusion, followed by warm wrappings; or by applying a hot flat-iron, combined with a mustard bath and subsequent warm wrappings. In the hæmorrhagic variety we must resort to general and local astringents. Ice, in every form of application or use, is an invaluable remedy.

The awful prostration of diphtheria is best combated by food, wine, diffusible stimulants, bark, and quinine, or iron. The antidiphtheritic serum should be injected hypodermically, its effect being closely watched.

The rheumatic affection of scarlatina is best treated like ordinary acute rheumatism, salicin and the salicylates being especially useful drugs for internal medication.

In acute desquamative nephritis, the patient, clad in a long flannel night-dress from head to foot, should remain in bed, wrapped in a blanket. He should be placed on a mild, unstimulating diet of milk, skimmed, or as buttermilk, farinaceous food, and light broths. Thirst is best relieved by copious draughts of cold water. Dry cupping and poulticing over the kidneys will do good. Local depletion by leeching, or wet cupping, may be practised with benefit in a robust patient. The bowels must be kept open by hydragogue cathartics. Should dropsy supervene, much benefit will be derived from hot air, vapour, or even warm-water baths. The wet pack may be used to promote elimination through the skin. To prevent uræmia, full doses of benzoate of sodium, with digitalis, should be given. If uræmic convulsions occur, a large dose of sulphate of magnesium, well diluted, or a bolus of calomel and jalap, may be administered.

Mercurials should, however, as a rule, be avoided in this affection. The temples may be dry-cupped, or leeched, and Trousseau's plan of compressing the common carotid artery in the neck, on the side opposite to that affected by the convulsions, may be tried. Other means of relief are chloral hydrate, with the bromides, butyl chloral, inhalations of chloroform, the nitrites, citrate of caffeine, diuretin, or an enema of black coffee.

In convalescence the patient should wear woollen clothing day and night, and in all seasons. The Jaeger system is both popular and efficient. Iron, quinine, and albuminous food are indicated in this stage. In diffuse cellulitis of the neck, early, deep, and free incisions should be practised, except in young children. The diseases of the ear in scarlatina require early and skilled attention. The external auditory meatus should be kept clean and free by gentle syringing. Douches and antiseptic or detergent gargles should be used. A single leech applied behind the ear relieves intense pain. A poultice may be afterwards applied, and the meatus stuffed with oiled cotton-wool.

<div align="right">J. W. MOORE.</div>

RUBELLA—ROSEOLA EPIDEMICA—RUBEOLA NOTHA.

Syn., Eng., *German Measles, Epidemic Rose Rash, Epidemic Roseola, Bastard Measles;* Fr., *Roseole;* Ger., *Rötheln.*

A SPECIFIC and infectious eruptive fever, distinct and separate, of its own kind; neither a hybrid of scarlet fever and measles, nor a modified form of one or other of those diseases, Rötheln breeds true. The disease begins suddenly, after an incubation of about twelve days, with ordinary febrile symptoms of moderate intensity. The rash appears on the first or second day. It consists of rose-red spots, sometimes so small and thickset as to resemble scarlatina, at other times larger and discrete, like measles. In some cases the rash presents both characters in different parts of the body. There are slight catarrhal and anginal symptoms. Enlargement and induration of the lymphatic glands in the occipital and cervical regions is a constant symptom. The febrile movement is brief, and recovery is generally uninterrupted and complete.

History.—The first British writer on this disease was Robert Paterson of Leith. He adopted the German name Rötheln, which is now being gradually superseded by the terms epidemic rose-rash and rubella. To old authors this eruptive fever was known by various names, of which roseola and *Erythème fugace* survive. The more accurate descriptions of the disease date from the middle of the last century (Orlow, 1758). Thomas described two epidemics of rubella, which occurred in Leipzig in 1868 and 1874. In the year 1874, also, an epidemic was observed in New York by Lewis Smith.

Etiology.—The assumption of a specific roseola is based chiefly on the fact that at certain times epidemics appear in which individual cases bear a causal relation to one another. Again, this disease affords no protection against either measles or scarlatina, whereas it does protect an individual from a second attack of itself. Lastly, it may attack those who have lately or previously passed through either measles or scarlatina. It is especially a disease of childhood, but may occur in adults up to the age

of 40. Very young children enjoy a certain immunity from it. Trousseau puts the case clearly and well when he asserts that rubella bears the same relation to measles and scarlatina that chickenpox does to smallpox. This is equivalent to saying that it is a totally distinct disease. As regards seasonal prevalence, rubella is generally most common in spring—March to June. In this particular it more closely resembles measles than scarlatina, which latter is an autumnal malady. It is infectious from the outset.

Morbid anatomy and pathology.— Analogy suggests that rubella is due to the presence of a specific micro-organism. Of its intimate nature we so far know nothing. The poison appears to have a special affinity for the lymphatic glands and skin. The mucous membranes are less actively involved.

Symptomatology.—*Incubation.*—This appears to vary widely in duration, but is probably twelve days, on an average.

Invasion.—The prodromal symptoms are sometimes absent or badly marked—attention being first drawn to the patient because a rash has been found upon the skin. Usually, however, the initial phenomena of a feverish attack are fairly in evidence. Nausea is a common symptom, and rarely convulsions may occur.

Eruption.—In a few hours, or on the second day, the rash appears on the body, thence extending to the legs. It may show itself first on the face and neck, down the back, or over the chest; most often it is like the rash of measles, less frequently it is scarlatiniform. The compound or hybrid rash has been seen by Küttner. It consists of minute red papules which coalesce and form larger irregular patches, without assuming the horse-shoe or crescentic shape of the rash of measles. The slightly raised rose-coloured spots or maculæ of rubella vary in size from a mere point to one-sixth of an inch in diameter. Troublesome itching accompanies the eruption, which fades slowly, leaving dark and dirty or yellowish stains visible for five, six, or more days.

Simultaneously with the rash, there is a mild injection and inflammation of the mucous membranes covering the buccal, pharyngeal, and nasal surfaces, and of the conjunctivæ.

Lastly, enlargement and induration of the lymph glands is an almost pathognomic sign of rubella. The glands on the mastoid processes, and behind the sterno-mastoid muscles, as well as those of the posterior chain below the occipital protuberance, are particularly affected. The bronchial glands almost certainly share in this pathological change.

Desquamation.—There is but little peeling in rubella. In several of my cases there was slight desquamation on the bridge and at the sides of the nose; in one case, the skin was shed in large flakes, as in scarlatina, and even the nails came off.

The febrile movement is usually slight. In three cases observed by myself, the maximal temperatures were 102°·4, 98°·2, and 99°·8 respectively.

Complications and sequelæ may almost be said not to exist in rubella. In one instance, profuse and repeated hæmoptysis seemed to have been brought about by caseation and tuberculisation of enlarged bronchial glands after an attack of this disease.

Diagnosis.—Rubella derives its chief importance from so often and so closely resembling measles or scarlatina. The subfebrile temperature of the early stage precludes the possibility of scarlatina and the probability of measles. The early appearance of the rash distinguishes it from that of

measles, while its usual "measly" character aids the diagnosis from scarlatina. The anomalous combination of the coryzal symptoms of measles, with the sore throat of mild scarlatina, should excite suspicion as to the probable presence of rubella.

From ordinary rose-rash, or roseola, and also from erythema, rubella is distinguished by its pyrexia, enlarged glands, and throat symptoms. The rash may be confounded with the early accidental rashes of smallpox, but the character of the prevailing epidemic and the subsequent history of the case should clear up the diagnosis.

Prognosis.—Once the diagnosis is made, we may, in most cases, pronounce an entirely favourable opinion. Yet rubella may occasion grave disturbance or even death in a delicate subject. The enlargement of the lymph glands also may have far-reaching and untoward effects upon the patient's health and constitution.

Treatment.—The patient should be kept in bed while the fever lasts, protected against cold, and suitably fed. Tepid or cool sponging will relieve itching. Watch should be kept upon any catarrh of the pharynx or air passages. Warm baths are most useful in convalescence. Good nursing and sound common sense alone are wanting to tide a patient over an attack of what has been called "this lightest of the acute exanthems."

<div style="text-align:right">J. W. MOORE.</div>

PERTUSSIS—WHOOPING-COUGH.

Syn., Old Eng., *Chincough;* Scots., *Kinkhost,* or *Kinkhaust;* Fr., *Coqueluche;* Ger., *Keuchhusten,* or *Keichhusten, Stickhusten;* Dutch, *Kinkhoest.*

AN acute specific disease of childhood in particular, highly infectious, running its course in six or eight weeks, seldom recurring, characterised especially by spasmodic fits of coughing, which often terminate in an attack of vomiting, and in the expulsion of a quantity of viscid mucus. The early symptoms are those of a common cold or catarrh, with some feverishness, but even in this stage the cough is harsh, brassy, and spasmodic. In and after the second week the paroxysms of coughing recur at longer or shorter intervals, and consist of a rapid series of forcible and noisy expirations, during which the face flushes, terminating in a prolonged shrill inspiration or whoop. Long after the disease has passed away, its peculiar cough may present itself in the course of an accidental "cold" or simple bronchial catarrh. Whooping-cough is apt to be complicated by bronchitis and catarrhal pneumonia.

History.—The earliest authentic notice of whooping-cough is said to date from the middle or towards the end of the sixteenth century. It was described by Sydenham under the names *Pertussis infantum* and *Tussis puerorum convulsiva.* Glisson called it *Tussis clangosa.* The Θηριώδης βήξ of Hippocrates and Galen was probably whooping-cough. Hoffmann translated this Greek term into Latin as *Tussis ferina.* As regards the Scots term, *host* means cough, and, according to Skeat, "a kink is a catch in the breath, nasalised form of a base *kik,* to gasp."

At the present day, whooping-cough is met with in nearly all parts of the habitable globe. Into Australasia and Polynesia it was introduced within comparatively recent times, even still it is of infrequent occurrence in

Iceland and the Faroe Isles. Its native habitat is by no means as extensive as its present geographical distribution. It is a fatal disease in badly nurtured children of tender years, particularly infants.

Etiology.—Whooping-cough occurs in frequent and either localised or wide-spreading epidemics, chiefly in spring and early summer (March to May or June)—at least in these countries. The outbreaks spread along lines of intercommunication and through schools, until they die out for want of fuel in the form of susceptible children. Other things being equal, the disease is less common and less severe in tropical and subtropical climates than in higher latitudes. Hirsch states that whooping-cough is independent of physical, social, and racial conditions. It is pre-eminently an epidemic disease. Outbreaks of whooping-cough have so often closely coincided with the prevalence of measles, as to suggest some causal relationship between the two maladies, which are said to hunt in couples. Such a relationship, however, has not yet been proved.

Girls are more prone to take whooping-cough than boys, and they also die of it in relatively greater numbers.

Although especially a disease of childhood, it is by no means unknown in adults up to 40 or 50. Hilton Fagge reminds us that an eminent London physician suffered from an attack of whooping-cough when more than 65 years of age. Heberden met with one case in a woman æt. 70, and another in a man æt. 80.

The bacteriology of whooping-cough is still obscure. Bürger says that elliptical cocci are constantly present in the expectoration of persons suffering from the disease. They are said to be easily brought into view by staining with fuschin or methyl-violet. Afanassiev isolated from the sputum of whooping-cough a short, thick bacillus, pure cultures of which produced, after inoculation in dogs and rabbits, symptoms resembling whooping-cough and broncho-pneumonia. Koplik found a very minute bacillus with rounded ends in thirteen out of sixteen cases of whooping-cough. O. Zusch described a bacillus which he found in the sputum of twenty-five children with whooping-cough. Be this as it may, infectious particles are certainly expelled with the cough from an early stage, and if these should reach the air passages of the susceptible, the disease is communicated to them. Fomites also play an important part in the diffusion of the malady. Hilton Fagge adduces a striking instance in which a boy in the early stage sneezed and coughed on a lady's dress while climbing upon her knee. Early next morning her own little daughter was found playing over the same dress, which had been laid upon an ottoman, with the result that exactly thirteen days afterwards this girl took ill and afterwards gave whooping-cough to two other children. The complaint has not been directly produced by inoculation.

Morbid anatomy and pathology.—Even assuming that the specific virus or poison of whooping-cough has not yet been identified and isolated, the extreme contagiousness of the disease, and the marked immunity which one attack bestows upon its victims, leave us no option but to assign it a place among the so-called zymotic or infective diseases. Numerous theories have been advanced to explain the phenomena of whooping-cough. A specific catarrh with hyperæsthesia is admitted by all. "One can easily imagine," says Hilton Fagge, "that the poison of this disease, having originally entered the air passages from without, and having set up a catarrh there, is during the prodromal stage conveyed to some part of the central nervous system, and there sets up the peculiar

spasmodic cough." The vagus nerve bears the brunt of the poisoning; hence the weak, quick pulse, the disturbances of respiration and of digestion, the tendency to hyperæmia of the lungs, the epigastric tenderness, and the spasmodic cough. This last-named and highly characteristic symptom may also be caused by a reflex peripheral excitement of the vagus due to the swelling of the bronchial glands in the spasmodic stage of the disease. Several causes probably co-operate in producing the disseminated pneumonia of whooping-cough. Extension of a bronchiolitis into the adjoining pulmonary lobules, vesicular hyperæmia from rarefaction of air in, and collapse of, the alveoli during the forced and repeated expirations, each plays its rôle; but, above all, we must regard the lesion in the lung as a true inhalation pneumonia.

Symptomatology.—We may consider the disease as it passes through its periods of latency, of invasion, of spasm, and of convalescence.

Incubation.—This is variable in length. Four days are assigned as its shortest, a fortnight as its longest, limit. Perhaps ten days may be regarded as its average duration—the same as measles. Towards the close of this stage, slight catarrhal and feverish symptoms may present themselves.

Invasion.—The invasion stage, or premonitory, prodromal, or catarrhal stage, commonly lasts a week. It may be entirely absent, or it may constitute the whole of the attack, the patient recovering in two, four, or five weeks, without more distinctive symptoms.

The onset of whooping-cough is gradual and insidious. The child is out of sorts, fretful, peevish; looks pale and ill, and does not eat. Temperature rises at night, sometimes considerably; sneezing and a harsh brassy cough set in towards evening, or on slight exertion, while the morning state is more satisfactory. The glandulæ concatenatæ in the neck enlarge. Examination of the chest reveals bronchial, dry, and moist sounds (rhonchi and râles), without dulness on percussion. The cough becomes worse and worse, more and more explosive in character; its paroxysms are more and more prolonged. At the same time, it does not "soften," nor is secretion expelled or swallowed, as in ordinary bronchial catarrh.

Spasm.—When the catarrhal stage has lasted for a week or ten days, the cough, instead of subsiding, becomes, except in mild cases, more and more convulsive in character, shows a disposition to occur in fits or paroxysms, and is often attended, or followed by, vomiting. Whenever a fit of coughing is imminent, the patient's face is seen to redden as he makes a vain effort to stifle or "smother" the cough, the only effect of which, however, is to hasten and intensify the attack. A quick succession of ten to twenty sharp, short, noisy, barking coughs of ever-increasing violence and boisterousness, culminates in a brief spell of apnœa. This is, in turn, rapidly followed by a loud, shrill, and deep crowing inspiration— the so-called "whoop," from which the disease obtains its name. Just before this forced and stridulous inspiration happens, the appearance of the patient betokens asphyxia; the face is livid, congested, and swollen, the veins stand out like cords, the eyes are bloodshot, the eyeballs seem about to start from their sockets, and now and then the nose begins to bleed.

Scarcely has such a fit of coughing passed off, when another like seizure begins. This may be equally severe, or shorter in duration, or less intense. And so the attack goes on, until, after several fits of explosive coughing, some more or less white, glairy, stringy mucus is discharged by expectoration or vomiting, or by both combined. Paroxysms like that

described may return only five or six times in the twenty-four hours, or they may mount up to as many as sixty to eighty. They are especially liable to take place at night. They cause great distress, and their approach is regarded by young children with terror. A child playing with his toys will suddenly stop in his play, and run to a bystander for help when he feels the attack coming on. Older patients describe a feeling of constriction in the throat, or a tickling in the larynx; infants look frightened, and become intensely restless as the seizure threatens.

At all times irregular in whooping-cough, the temperature in this spasmodic stage varies. Usually it is normal, or nearly so, while the pulse remains rapid. But if the spasms, through their frequency and intensity, induce disseminated broncho-pneumonia, or catarrhal pneumonia, considerable fever may develop, and the temperature may rise to 104° F., or even higher.

When the child is very young, and the fits of coughing are frequent and severe, grave symptoms develop. These are—duskiness of the face, cyanosis, œdema of the face and neck, bloodshot eyes, nose-bleeding, blood-stained expectoration, deafness from rupture of the membrana tympani, escape of blood from the ear or ears, squinting, temporary loss of sight during the fit, transient albuminuria, spasmodic movements of the face muscles, and general convulsions, ending in coma and death.

Exhaustion for a while follows a paroxysm, or headache is complained of; the child, however, soon regains its wonted cheerfulness, and asks for food, especially if he has vomited.

The complications which may accompany the spasmodic stage are: Bronchitis, of varying degrees of intensity and extent; pneumonia of the catarrhal type, and lobular in distribution; collapse of the lung; pleurisy, which may end in empyema or pyothorax; pulmonary emphysema, rarely general emphysema or pneumothorax. Samuel West has recorded a case of right hemiplegia with aphasia and athetosis, probably due to cerebral hæmorrhage during a paroxysm in whooping-cough. Hilton Fagge mentions ascending paralysis as a rare sequela, and perhaps depending on peripheral neuritis. In this stage, also, probably as the result of mechanical chafing against the teeth, or even the gum, in a toothless infant, one or more shallow sore ulcers form upon the frænum linguæ, or alongside it on the under surface of the tongue. These were first described by Bouchard and other continental writers; but, in this country, attention was first drawn to them by Thomas Morton. The sublingual ulcers were met with by Morton in about 40 per cent. of his cases, generally between the third and fifth week, so that their recognition aids the diagnosis.

Decline and convalescence.—After a fortnight or so of violent fits of coughing, the intensity of the attacks lessens, the intervals between successive paroxysms lengthen, the secretion of the bronchial mucous membrane becomes looser, and is more easily got rid of, and the patient shows evidence of returning health and strength. The least indiscretion or want of care may in this stage cause a relapse, or induce some pulmonary complication. In favourable cases, convalescence is completed within six weeks from the onset of the attack. In other cases, the disease may last two months, or longer, and convalescence may be very protracted, particularly in winter. Caseating bronchial glands and deposits in the air vesicles of the lungs again may pave the way for tuberculous infection and resulting pulmonary phthisis. Tuberculous meningitis and acute tuberculosis are rapidly fatal sequelæ.

Diagnosis.—In the early or prodromal stage, whooping-cough may be confounded with a simple catarrh, or with epidemic influenza. In all cases, attention should be paid to the prevailing epidemic. Influenza attacks persons at all ages, comes on suddenly, with rheumatoid pains, high temperature, and often nervous or gastric symptoms. Children affected with influenza do not whoop. Simple catarrh and bronchitis are especially diseases of winter. When suffering from them, children do not, as a rule, expectorate or vomit, and these affections are directly attributable to exposure to cold or a wetting, while they come on suddenly, and are early attended by hoarseness from laryngitis.

Hay fever or summer catarrh occurs in early summer, when the air is laden with the pollen of grasses and of various shrubs and trees. The malady affects adults rather than children, and only a certain number of individuals are prone to it. Hysteria is sometimes accompanied by a spasmodic, hard, brassy cough, which is, however, incessant, and unattended by the characteristic whoop. Hysteria affects girls and young women; is independent of season, and is infectious only by imitation—it is a mimetic neurosis.

Prognosis.—Whooping-cough is a dangerous malady in infancy, in badly-housed and badly-nourished children, and in those who are rickety. It is naturally more fatal in winter and spring than in summer and autumn. According to the United States Census Reports, it is more than twice as fatal in the negro race than in others. A paroxysm seldom kills, but it may cause death in a very young child through complete closure of the glottis, perhaps from syncope, or through the rupture of an intracranial blood vessel. Fatal coma may supervene where the paroxysms are frequent and violent. Convulsions are most dangerous in any stage of the disease. It is, however, to the concurrent bronchitis and pneumonia of whooping-cough that the majority of the fatal cases are due. The accidents of pulmonary emphysema and collapse often end in recovery, probably because of the youth of the patients. On the other hand, caseation of the deposits in the pulmonary alveoli, or of the unresolved bronchial and mediastinal glands, supplies a fertile soil for the *Bacillus tuberculosis*. Lastly, convalescence is often delayed by fresh catarrhal attacks in cold weather, or by continued loss of appetite.

In England and Wales the deaths from all causes in the ten years, 1881–90, gave a death-rate of 19·08 per 1000 of the population annually. The corresponding figure for whooping-cough was 0·45 per 1000. The fatal cases of this disease at all ages amounted to 123,597 in the decade. Included among these deaths were 119,200 of children under 5 years of age. Under 1 year, 53,407 died; between 1 and 2 years, 37,774; between 2 and 3 years, 15,299; between 3 and 4 years, 8,292; between 4 and 5 years, 4,428.

Treatment.—So far no specific for whooping-cough has been discovered. Fresh air is the nearest approach to a specific which we at present possess; but in using it we must not unduly expose our patient— a child, sensitive to cold in more ways than one, for the exposure may bring on a paroxysm or, still worse, induce an attack of bronchitis. In fine weather, however, open-air exercise may be allowed. At other times a warm equable temperature and a large airy room are essential. Towards convalescence, change of air, particularly to or near the seaside, hastens recovery. The diet should be light and nutritious, consisting largely of milk, animal broths, and egg puddings. The meals should be given at

shorter intervals than in health, and, if possible, after the several paroxysms of cough, so as to ensure that they will not be ejected by vomiting. All excitement must be avoided, for undue talking, crying, or laughing may bring on a fit of coughing.

The air of the room occupied by the sick child or children may, with benefit, be impregnated with a disinfectant, such as turpentine, carbolic acid, creosote, guaiacol, sulphurous acid gas—the last, in particular, appears to possess direct curative properties, and the patients soon come to bear quite a concentrated atmosphere of it. Thiocamf may be substituted for sulphurous acid. It is a liquid combination of sulphur dioxide, camphor, and various volatile aromatic bodies.

As regards the internal administration of drugs, little need be said. A sip of cold water now and again often allays cough and is grateful to the sufferer. In the catarrhal stage, a simple mixture of ipecacuanha wine with solution of citrate or acetate of ammonium, glycerin, and water, gives relief. Cherry laurel water, or minim doses of dilute hydrocyanic acid, may be prescribed in combination with one or more of the bromides. The chest should be gently rubbed with a liniment of chloroform and camphor of moderate strength, and afterwards poulticed with linseed meal or wrapped in wadding under oiled silk, or covered with Gamgee tissue.

In the spasmodic stage, in addition to the foregoing, we may order chloral hydrate and quinine—1 gr. of the latter per diem in powder for each year of age, continued for two or three days only. Alum is recommended (1 to 5 grs. every four hours) in this and the final stage, or the addition of compound tincture of camphor to the ipecacuanha wine, one part to two for young children, two parts to one in chloroform water in adolescence. Inhalations of nitrite of amyl are of use in spasm. Belladonna is often given in combination with carbonate of potassium—10 minims of the tincture thrice daily is the dose for a child of 3 years. Hydrochlorate of cocaine ($\frac{1}{16}$ gr. to $\frac{1}{4}$ gr. thrice daily) is favourably spoken of by Goodall and Washbourn, while several writers have testified to the great utility of bromoform in controlling the paroxysms and relieving vomiting. The capsules of bromoform contain a half or one minim dissolved in oil. Bromoform may also be dropped upon a lump of sugar or into water, or it may be given in combination with alcohol, as suggested by Carpenter—

R

Bromoformi	.	.	.	.	♏xlviij
Alcohol	.	.	.	.	℥ss
Tinct. cardamomi comp.	.	.	.. ad ℥iij

M.

Signa.—Shake the bottle. A fluid drachm three times a day in water.

J. W. MOORE.

MUMPS—EPIDEMIC PAROTITIS.

Syn., Scots., *The Branks;* Lat., *Angina maxillaris vel parotidea, Cynanche parotidea;* Fr., *Oreillons, Ourles;* Ger., *Ziegenpeter, Bauerwetzel.*

An acute, specific, and infectious febrile disease, characterised by inflammation of the salivary glands—especially the parotid gland—often assuming an epidemic form, occurring as a rule once only in a lifetime, and supposed to be propagated by means of the breath and saliva.

The testes in the male, the external genitals and mammæ in the female, are sometimes involved in the specific inflammation of mumps. The ovaries are very rarely, if ever, engaged. These metastases usually take place when the parotid symptoms are declining. The disease is in general not dangerous to life; but if suppuration occurs, the mastoid cells may become implicated, leading to meningitis or to pyæmia.

History.—Hirsch tells us that epidemics of inflammation of the parotid gland were long ago described in a masterly fashion by Hippocrates, who also pointed out the fact, observed by himself, that swelling of the testicle may occur in the course of the disease. Mumps is found in all countries and in all climates, no part of the habitable globe being exempt from this strange malady. It occurs either in circumscribed outbreaks in schools or barracks, or in widespread epidemics. Many records exist of the prevalence of mumps among troops in garrison or in the field, and it occasionally breaks out on board ships of war. In the American War of 1862–65, mumps occurred to a notable extent, particularly in the first year of the war, when forty cases were reported among every 1000 men. Of 48,128 cases reported altogether, seventy-two died.

Etiology.—No doubt exists as to the contagiousness of mumps. It is certainly an infective disease. Its exciting cause would seem to be a micro-organism discovered by Michaelis. In 1897, Bein described this micro-organism as a streptococcus, very similar in its shape and in its attitude in the cells to the gonococcus and to the meningococcus. It grew in ordinary agar, peptone bouillon, and ascitic fluid. It curdled milk and liquefied gelatin. Its movements were peculiar. Fresh cultures would kill mice. It had been found in the secretion from Steno's duct, in the contents of parotid abscesses, and once in the blood.

The prevalence of the malady is favoured by cold and wet. Its epidemics generally arise in winter after spells of cold, wet weather, and its victims are principally those who have been most exposed to such weather. Children, other than infants, and soldiers show a singular predisposition to mumps. It is, however, met with at all ages, and some years ago I observed an instance in which an adult maid-servant infected a family of young children, from whom their aunt and grandmother subsequently took the disease. Boys are more prone to catch the disease than girls. Mumps has not infrequently been epidemic at the same time as certain eruptive fevers, particularly measles and scarlatina. This appears, however, to be a mere coincidence. The infection clings to a patient for two or three weeks after the parotid gland swells.

Morbid anatomy and pathology.—As regards the local lesion, the inflammation would appear to fall much more heavily on the connective tissue stroma of the parotid and salivary glands than on the acini of these glands themselves. It involves also the connective tissue elements which surround the glands; in a word, we have to deal with an interstitial rather than a parenchymatous inflammation. Cellulitis occurs and may spread to neighbouring lymph glands.

Symptomatology.—The stage of incubation lasts for one week to three weeks. It is generally about a fortnight. The initial or prodromal symptoms are—a feeling of fatigue, chilliness, gastric derangement and vomiting, and restlessness at night. Then the temperature rises to 100° or 101° in most cases, to 103° or 104° in others. Aching pain and swelling soon set in at one side of the face, involving the parotid and submaxillary glands. The pain sometimes resembles toothache, at other times it is

absent, or it consists in a feeling of stiffness and discomfort about the jaw, with inability to open the mouth wide or to chew solid food. Yawning gives great pain, and even speaking causes distress. A swelling quickly appears at this time under one ear. It spreads backward under the sterno-mastoid muscle, forward to the angle of the jaw, and downward along the side of the neck. The tumour displaces the lobe of the ear. It feels elastic, is slightly softer in the centre, but does not pit on pressure. Over it, the skin is tense, shining, and swollen, pale in colour and waxy-looking, but occasionally showing a red blush. Salivation may accompany the swelling, but frequently the secretion of saliva is unaltered in quantity or quality, sometimes it is diminished. There may be hardness of hearing on the affected side. Tinnitus aurium also occurs, or complaint may be made of shooting pains in the ear or ears. In some cases the swelling is limited to one side, in others both sides are attacked together. Most usually, as the swelling of one side begins to go down, the other side becomes affected. Pyrexia ceases about the fourth day. The tonsils and neighbouring parts may swell in mumps. The breath has often a heavy, fœtid smell.

The tumefaction subsides as quickly as it developed, so that absorption is completed in three or four days. The whole duration of the attack varies from a week or ten days to a fortnight.

The skin occasionally peels over the affected parts, especially when they have been poulticed or fomented.

Complications are rare. The most common is the so-called "metastatic" orchitis of boys and young men. This comes on as the face troubles decline. The right testicle is credited with being most frequently affected. Temperature rises again, so that high fever and delirium may appear. Collapse occurred in a man æt. 35 under Trousseau's care; but yielded to treatment, and especially to the development of a metastatic orchitis. In another case observed by him, that of a lad æt. 17, the typhoid or ataxic state developed, but gave way on the supervention of swelling of the scrotum and one testicle. Orchitis in mumps lasts from three to six days, and then quickly subsides. It may, however, lead to permanent atrophy of the testicle, or epididymitis may develop. Morton long ago described cases of this kind under the expressive term, *Febris testicularis*.

Acute otitis may rarely occur. Also, very rarely, ophthalmia. Hilton Fagge further mentions acute bronchitis, bubo, and urethritis as occasional complications of mumps. Zinn reports a case of endocarditis in a boy æt. 13. To these should be added mastitis and œdema of the vulva in girls.

Diagnosis.—Mumps is easily recognised. From faceache it is distinguished by its sharp fever and the development of the parotid swelling. Occasionally a secondary or metastatic parotitis occurs in the course of severe enteric fever or other acute infective disease, and in 1887, Stephen Paget drew attention to the occurrence of suppurative parotitis in abdominal and pelvic diseases. In 1892, the same surgeon reported a case of abdominal section followed by parotitis. But, in all these, early suppuration takes place in the inflamed parotid gland. The cervical swelling in diphtheria may be mistaken for mumps; but examination of the mouth and throat should solve any difficulty in diagnosis.

Prognosis.—Mumps is a comparatively trivial disease, in the absence of any constitutional delicacy or tuberculisation. In rare instances, secondary meningitis has destroyed life, after suppuration had occurred, involving the mastoid cells. This train of events was demonstrated during the course of

the American War of 1862–65. It should not be forgotten that atrophy of the testicle may be a sequela in a case of metastatic orchitis.

Treatment.—Rest in bed during the febrile stage is judicious at all times, it is essential in winter. The patient should in any case remain in a warm, equable atmosphere until the parotid swelling has entirely subsided. Metastasis is apt to occur after exposure to cold and wet or from over-fatigue in convalescence.

As the patient cannot masticate, nourishing broths, jellies, milk preparations, and whipped-up eggs should be ordered. Ice is very refreshing and useful. Attention should be paid to the state of the bowels, and rest at night should be secured by Dover's powder, or by chloral and bromide draughts, or some other means. The simplest application to the swelling is a pad of Gamgee tissue or French wadding under oiled silk. Warm fomentations also give relief—infusion of chamomile or decoction of poppies may be used for the purpose. Should suppuration threaten, free poulticing will be of service. Tepid sponging all over the body, or even a warm bath, is grateful and soothing. The bath should always be resorted to when metastasis is suspected. In convalescence, tonics like iron, quinine, arsenic, strychnine, and cod-liver oil are indicated.

<div align="right">J. W. MOORE.</div>

INFLUENZA—EPIDEMIC CATARRHAL FEVER.

Syn., Lat., *Catarrhus epidemicus ;* Fr., *La Grippe ;* Ger., *Epidemischer Schnupfenfieber.*

INFLUENZA is a very acute, specific, infectious febrile disease. Its virus or contagium, when once introduced into the body, presumably by inhalation, acts primarily and quickly on the nervous system, producing the symptoms of an acute pyrexia, with remarkably rapid pulse. The malady is undoubtedly contagious, but its incubation stage is singularly short. Its outbreaks are so sudden and often so widespread, affecting multitudes at one and the same moment, both by sea and land, as to suggest a miasmatic origin. Viewed in this light, the micro-organisms concerned in the production of the disease may possibly undergo multiplication and development in the atmosphere itself, so causing the pandemic rather than epidemic prevalence of the malady. Very young children seem to enjoy a certain immunity from influenza, or to have it in a mild form—as an ephemeral fever, followed by profuse sweating, and, after a few days, a tendency to slight catarrh.

Influenza, while infrequently directly fatal, causes an indirect loss of life which is appalling, chiefly through complications affecting the respiratory and, in advanced life, the circulatory systems. It has been said that influenza, while relatively less fatal, is absolutely more fatal, than cholera.

Influenza is a perilous complication of pulmonary consumption. It seems to have the property of picking out the weak point in an individual's constitution. It shows a marked tendency to relapse, and to this is largely due the indirect fatality of the malady. The febrile movement in even uncomplicated influenza is polytypical or atypical—that is, it presents many varieties and is not characteristic. It lasts from two to six or seven days. Fever is occasionally entirely absent. Unlike most of the

other acute specific diseases, influenza confers no immunity against future attacks.

History.—The earliest authentic notices of influenza date from A.D. 1173, in December of which year there was an epidemic in Italy, Germany, and England. Numerous outbreaks subsequently took place either as pandemics or as circumscribed epidemics, from time to time down to 1847, in the late autumn and winter of which year the disease became generally diffused over the Eastern Hemisphere. Epidemics occurred still later in 1850–51, 1855, 1857–58, and 1874–75, but none of these visitations produced a deep impression on the medical mind, and the British Isles in particular almost escaped them. It thus happened that, when the so-called Russian influenza swept westward across Europe, towards the close of the year 1889, the malady presented itself as practically a new and unknown disease to the vast majority of the physicians who were called upon to treat it, and whose experience did not go back to the memorable outbreak of 1847. Since 1889, successive waves of influenza have surged across both the Eastern and Western Hemispheres, and now (1899) the terms influenza and *Grippe* are as familiar as household words in all parts of the world.

Etiology.—In 1892, a bacillus was discovered by Pfeiffer, and independently by Canon, which is believed to be the specific cause of influenza. Pfeiffer detected the bacillus in the purulent bronchial secretion, Canon in the blood, of influenza patients. Its presence in the blood is not established by the experience of observers other than Canon.

The *Bacillus influenzæ* is very minute, about $0.5~\mu$ in length and $0.2~\mu$ in diameter—that is, half as long only as Koch's bacillus of mouse-septicæmia, but the same thickness as that micro-organism. It is aërobic, non-motile. Spore formation has not been observed. It is solitary or united in twos, resembling diplococci, or in chains of three or four elements. When cultivated, these bacilli grow well in broth and on the surface of glycerin agar at 37° C. (98°·6 F.). They do not thrive at temperatures below 28° C. (82°·4 F.) (Klein). Kitasato considers that they are a definite species, not occurring in any disease except influenza. The bacilli are quickly destroyed by desiccation. The thermal death point is 60° C. (140° F.) with five minutes exposure.

Pfeiffer infers that this bacillus is the specific cause of influenza in man, because it was found in all uncomplicated cases of influenza examined, in the characteristic purulent bronchial secretion; often in the protoplasm of the pus corpuscles, and (in fatal cases) in the peribronchial tissue and on the surface of the pleura; it was found only in cases of influenza; the presence of the bacillus corresponded with the course of the disease, and it disappeared with the cessation of the purulent bronchial secretion.

Having regard to the clinical history of influenza, it is hard to believe that the disease is only contagious and not also air-borne. To use an expression familiar to the physicians of the sixteenth and seventeenth centuries, the virus of influenza would seem to cause a fouling of the air or miasma, from which its pandemic outbreaks presumably take their rise.

In a word, Pfeiffer's *B. influenzæ* is perhaps a facultative parasite —that is, it can exist independently of a living host as a saprophyte, although it usually plays the rôle of a true parasite.

Of course it is not denied that the morbific agent or virus is capable of clinging to the human body, or to clothes or luggage or letters, so as to be conveyed by them from place to place. "But," says Hilton Fagge,

"its subsequent growth and development is doubtless altogether independent of this kind of assistance." The prevalence of the disease is uncontrolled by season or weather.

Morbid anatomy and pathology.—The causal relationship of Pfeiffer's bacillus to influenza must be admitted. In addition to that specific micro-organism, the *Diplococcus pneumoniæ*, the *Streptococcus pyogenes*, the *Staphylococcus aureus*, and the *Staphylococcus albus*—all play more or less important though subordinate parts. To their presence many of the complications of this Protean disease are due. The post-mortem appearances are referable in the first place to influenza itself; in the next place, and chiefly, to its secondary complications and sequelæ. Like other acute specific infective diseases, influenza causes parenchymatous degeneration of the liver, kidneys, and spleen, as well as of the muscular substance of the heart, and of the minute vessels.

Symptomatology.—Influenza sets in with extreme suddenness and violence—it may be only a few hours after exposure to infection. In most, if not in all cases, there is an interval between the reception of the poison and the development of the symptoms. The most usual duration of this interval seems to be one or two days. In the epidemic of 1889–90, I observed many cases of apparent communication of influenza from person to person, but without being able to calculate accurately the duration of the period of incubation. In one such instance, however, a lady visited a friend ill of influenza at 2 P.M., and was, three hours later, attacked with symptoms of the disease—chills, weakness, coryza, lachrymation, stuffing of the nostrils, and loss of smell and of taste. Here, doubtless, the virus clung to the person or dress of the first patient, and was received into the system of the second, producing its toxic effects almost at once.

Adults suffer severely in many cases, the symptoms being chills, headache, often sleeplessness, sometimes delirium; pains in the eyeballs, nape of the neck, small of the back, knees, and along the margins of the ribs; loss of the special senses of smell, taste, and sometimes hearing; smarting of the eyes, photophobia, lachrymation, otalgia; complete loss of appetite, thickly-coated tongue, bad taste in the mouth, foul breath, nausea, and perhaps vomiting; constipation, but occasionally diarrhœa; cough, frequent sweating, loss of strength, fainting. Of course it is only a selection from these symptoms that is present in a given case.

While a constitutional malady, influenza in individual cases spends its violence on one or other of the great systems of the body. Hence it presents several well-marked clinical varieties, or types, such as (1) the nervous, neuralgic, or rheumatoid type; (2) the catarrhal and cardio-pulmonary types; (3) the gastric type; (4) the febrile type.

The nervous type.—One of the earliest cases which I saw in the epidemic of 1889–90, belonged to this class. The patient was seized on the evening of Friday, December 20, 1889. The following is the lady's own account of the attack :—

"*Friday, 20th December* 1889.—I went to the oratorio at St. Patrick's Cathedral, apparently in my usual health. Shortly after entering the Cathedral I felt chilled, as if cold water was being poured down my back and legs. When I returned home I warmed myself at a good fire, was given some hot wine and water, and went to bed; then my face and head got very hot and uncomfortable, and pains began in my arms, shoulders, and legs. All night the pains were very bad, sometimes so sharp across

the back of my chest that I could have cried out; and although I felt burning to touch, the cold-water sensation continued. I got no sleep that night. Next day, about twelve o'clock (mid-day), I was given a powder (salicylate of sodium), and in two hours afterwards another, which put me into a perspiration. The pains in my limbs got better, but my head began to ache badly, and all day I felt very ill. I suffered from great thirst. Saturday night slept better. Sunday morning, about 5 A.M., I wished for a cup of tea, but could not taste it. I might as well have been drinking hot water. Sunday evening pains had quite gone. I had no headache. I got up for a while, but felt very weak. For several days I had no energy for anything, the least exertion tired me. My sense of taste did not return for four or five days. I also got a cough which was very troublesome. Temperature—Friday night, 101°; Saturday morning, 100°; evening, 98°·8."

The nervous symptoms of this form of influenza arrange themselves under the headings—rheumatoid and neuralgic pains in the head, back of the eyeballs, small of the back, limbs, and joints; lesions of sensation, including loss of the senses of taste and smell; various paralyses, should peripheral neuritis or myelitis occur as a complication; heart failure, and muscular prostration. The patients are often sleepless and delirious, and the temperature runs rather high for three or four days. Profound depression and anæmia are common in the protracted convalescence of this type, and relapses are very apt to take place even more than once. In convalescence, the powers of the mind may be shaken—acute mania developing, with a suicidal impulse; or more chronic depression of spirits and melancholia.

Cardio-pulmonary type.—On Monday, 30th December 1889, Mrs. W., a lady, æt. 54, somewhat frail and delicate, while out walking was seized with shivering and violent headache, and intense pain in the back and in the "bones." On reaching home she at once went to bed, feeling very ill and prostrate. Next day I visited her. The tongue was thickly furred and dry. Her pulse was 132, respirations 28, temperature 103°·3. Having regard to the sudden onset of the illness and the symptoms, I pronounced the attack to be one of influenza.

On the third day the pulse was 110, respiration 28, temperature 102° F. The tongue thickly coated; eyes tender, and lachrymation; complete anorexia; great prostration.

January 2, 1890 (fourth day).—The report was that she had a better night. Herpes was showing round the nostrils. Pulse, 96 to 100; respiration, 28; temperature, 102°·4. Severe stabbing or catching pain was complained of at the lower part of the left side of the chest. No physical signs could be detected, and a poultice relieved the pain.

January 3 (fifth day).—Pulse, 110; respiration, 32; temperature, 102°·7. A lymphy crepitation was now audible over the upper part of the left side of the chest, and on deep inspiration a fine pneumonic crepitation could be heard.

January 4 (sixth day).—Pulse, 110; respiration, 40; temperature, 103°·3. Dulness now existed, which was rapidly extending all over the left apex, where also a marked *frottement* could easily be recognised. At 6 P.M., Dr. Watson Pike saw the patient with me, and agreed in my diagnosis of influenza complicated with a left pleuro-pneumonia. Pulse, 112; respiration, 42; temperature, 102°·7. There was not a trace of expectoration, and scarcely any cough occurred. We considered the patient to be in danger, and continued the treatment, which consisted in free stimulation, frequent feeding, and quinine.

At 1.30 A.M. on *January* 5, I was summoned to see the patient, and found her sinking fast. Dr. Hearn of Rathmines kindly joined me in consultation. Her pulse was failing, and the temperature was 103°·3. She rallied for a time, but at 6 A.M. another attack of cardiac failure came on. From this also she rallied, but at 10 A.M. she suddenly died. The temperature chart (Fig. 29) gives the facts in this case.

As bearing on the diagnosis of this case, it is to be noticed that four—if not five—of the other members of this lady's family suffered from influenza either immediately before or after her illness.

Many of the cases classed under the heading of catarrhal influenza develop symptoms of catarrh, of the various mucous membranes lining the respiratory tract, at the outset. The affection extends into the bronchioles and adjoining pulmonary lobules, constituting a broncho-pneumonia, or catarrhal pneumonia. In many other instances, however, a lobar pneumonia ushers in the attack. This would seem sometimes to be caused by a secondary infection by the *Diplococcus pneumoniæ*, more commonly by a secondary infection by the *Streptococcus pyogenes*—an etiological fact which
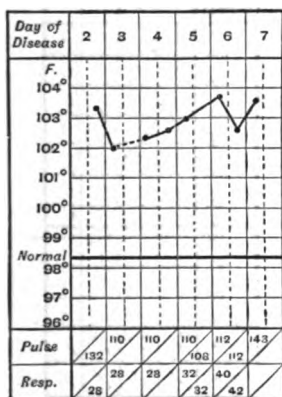
FIG. 29.—Influenza—Cardio-pulmonary.
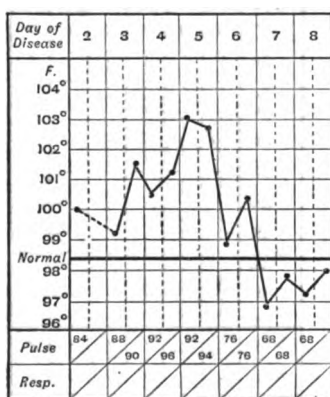
FIG. 30.—Influenza—gastric.

would explain the many-celled purulent expectoration, which so often takes the place of the viscid rusty sputum of ordinary lobar pneumonia.

Gastric type.—On Wednesday, January 8, 1890, Mr. W. B. S. enjoyed a day's shooting in the Co. Wicklow. The following day he returned to town in his usual good health; but in the afternoon felt chilly, complained of headache and nausea, and felt utterly miserable. He went to bed early, but passed a wretched night—restless and sleepless. Next morning I found him complaining of pains in the eyeballs, back of the head, and small of the back. Pulse, 84; temperature, 99°·9; tongue thickly coated; complete loss of appetite and nausea. He felt entirely prostrate, and, at my evening visit, expressed his belief that some fish which he had eaten for dinner had thoroughly disagreed with him. Two miserable days of sickness followed, the temperature rising on the morning of the fifth day to 103°·1. A short cough had set in, and the eyes were suffused and tender. There was constipation, and he complained of weight and fulness in the pit of the stomach. Dr. James Little saw him with me, and thought it likely that the fever would run on for some time. A quiet day gave promise of a restful night, and this promise was abundantly fulfilled. He had an excellent night, partly due to 20 grs. of phenazone (antipyrine), with

20 minims of tincture of gelsemium in a draught, in divided doses at bedtime. Next morning, pulse, 76; temperature, 98°·7, rising to 100°·2 in the evening, but without any return of restlessness. Subnormal temperatures followed for a few days—96°·4 being one observation. The tongue cleaned very slowly, and several days of extreme languor and weakness preceded final convalescence. Fig. 30 includes the observations in this case.

This gentleman's wife had, a few days previously, suffered from influenza, from which she was recovering when he fell ill. She nursed him, and got a relapse, accompanied with cough, bronchial catarrh, and absolute loss of appetite.

Dawson Williams points out that children in particular suffer from the gastric form, and that, in them, a sudden attack of vomiting is followed by diarrhœa, the stools being not infrequently blood-stained. There is extreme prostration. In a case observed by myself in January 1890, a boy of 7½ years had incessant vomiting and nausea for twenty-four hours, as well as profuse sweating, with a pulse as fast as in scarlet fever—140
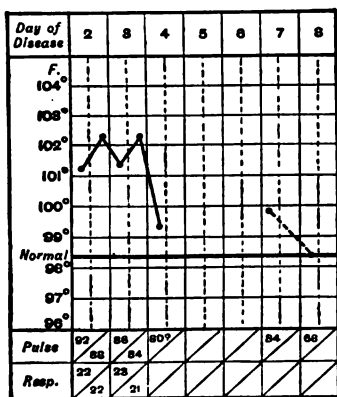
FIG. 31.—Influenza—febrile.
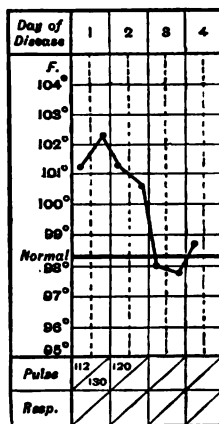
FIG. 32.—Influenza in child.

per minute. Peacock, in his account of the epidemic of 1847, drew attention to the frequent presence of slight jaundice, nose-bleeding, and albuminuria.

Febrile type.—On New Year's Eve, 1889, I received a note from a surgical colleague asking me to see him, as he had been taken ill the same afternoon while in his study. On visiting him in bed, he was still shivering at times, and complaining of a distressing feeling of cold water streaming down his back. He stated that he had been out of sorts for three or four weeks, and it was quite evident that he had made up his mind that the attack was one of typhoid fever. His pulse was 92, the temperature about 100°. His tongue was very furred, and his eyes were injected, with swollen lids. He had lost the sense of taste and smell, and complained much of rheumatoid or neuralgic pains in the back and limbs. Two restless feverish nights followed.

There was in this case steady pyrexia for four days, and then came profuse sweatings, lasting for several days. A slight elevation of temperature occurred on the evening of the seventh day, after which convalescence went on uninterruptedly. The weakness was for a time extreme.

This febrile type prevailed especially among children. In three charts,

showing the febrile movement in girls, aged from 12 to 15, the marked subnormal temperatures on the third and following days are very noteworthy, and are so constantly present in the defervescing stage of influenza as to become an important diagnostic sign. The charts (Figs. 31–34) illustrate the fever movement in influenza as it attacks children.

Complications.—I have seen fatal cases of influenzal bronchitis, pneumonia, pleuritis, and heart failure. The pneumonia, while producing the ordinary physical signs of acute croupous pneumonia, is often latent in its course, or accompanied by a profuse muco-purulent expectoration, with scarcely any rusty sputa. The ebbing of the strength in some of these cases in elderly people is something awful—it is often absolutely beyond control. Other complications of which I have had experience are: Epistaxis, facial neuralgia, profuse sweatings, skin rashes, and cystitis, followed by mild orchitis.

In contrast to dengue fever, influenza is a non-eruptive fever. When
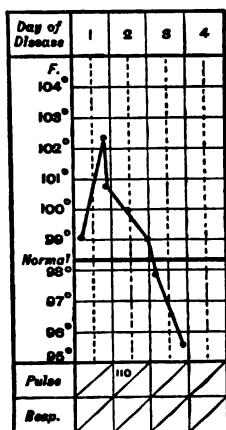
FIG. 33.—Influenza in child.　　FIG. 34.—Influenza in child.
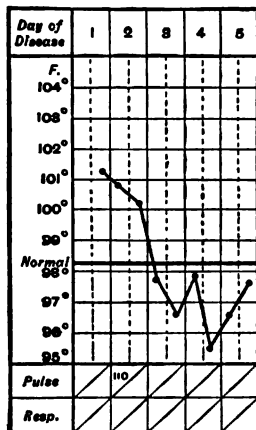
rashes do appear, they are accidental rather than essential or specific, and they result from hyperpyrexia or profuse sweating, or from the ingestion of such drugs as quinine, or phenazone, or salicylate of sodium.

Diagnosis.—Influenza has been looked on as a variety of dengue, which, however, is an eruptive fever more closely resembling scarlatina, and prevailing only in tropical or subtropical climates.

When *typhoid fever* sets in suddenly, the symptoms closely simulate those of influenza. The subsequent course of the fever is quite different. Regard should be had also to the prevailing epidemic, and to the patient's surroundings. The application of Widal's test might materially aid the diagnosis.

The *pneumonia* of influenza is more prostrating than ordinary pneumonic fever. The rusty sputa of the latter are usually wanting, the sputa are rich in young cells, they are muco-purulent or purulent.

The onset of *smallpox*, with its backache, vomiting, nausea, and foul tongue, may resemble influenza; but the course of the two diseases is entirely different, and due weight should be given to the prevalence of either disease at the time.

A *common cold* is not so severe, or so prostrating, as influenza.

Prognosis.—Influenza is not *directly* a very fatal disease. In the

epidemic of 1847, the death-rate was estimated at 2 per cent. of the cases observed in London. It has probably not been higher in the outbreaks of 1889 and more recent years. An epidemic of influenza, nevertheless, produces a startling and excessive increase in the death-rate. In 1889–90, influenza was more pernicious to the population of Dublin than the extreme cold of January 1881, or of February 1895. It slew its victims, not so much directly, as by means of complications and sequelæ affecting the breathing organs and the heart. It spared the lives of children of tender years, but killed large numbers of adults and those advanced in life. According to the registrar-general for England, the deaths directly attributed to influenza in England and Wales during 1890 numbered 4523, but he estimates the number of deaths directly and indirectly due to it at 27,000, equivalent to an annual death-rate of almost 1 per 1000. The subjects of heart disease and of phthisis die off like flies when attacked by this affection.

It should not be forgotten that influenza predisposes not only to acute pneumonia, but to tuberculosis, and that months may elapse before the shaken powers of mind as well as body are fully restored after an attack.

Treatment.—The management of influenza turns upon common-sense principles. In the first place, "prevention is better than cure." The treatment is expectant, palliative, and symptomatic. There is no specific for this strange malady, but the physician, notwithstanding, may do much to aid his patient towards recovery, to assuage his suffering, and to prevent or control complications. To struggle against his illness is supreme folly on the part of an influenza patient. On the contrary, he should take to his bed immediately on becoming aware that he is attacked. During the acute stages, only light fluid nourishment should be allowed, at rather frequent intervals—every two hours or so. Chicken-broth, milk and soda-water, acidulated barley-water, toast-water, two-milk whey, combined with equal parts of egg-water (that is, white of egg whipped up and mixed with cold water in the proportion of two to four whites to a pint of water, and strained),[1] or white-wine whey only should be allowed, so long as the temperature is high and the stomach is irritable. Afterwards an abundant supply of nutritious and digestible food will be needed, as well as stimulants in the case of elderly patients.

Solution of the acetate or citrate of ammonia is recommended as a mild antipyretic in the early stage. A warm bath, with strong solution of ammonia added to the water, relieves the distressing feeling of chilliness at the outset. Quinine, in moderate doses of 2 or 3 grs. thrice daily, usually agrees, and is useful. The torturing pains readily yield to phenazone (antipyrine); but the remedy should be exhibited in small doses, and not pushed. A most useful formula is the following:—

  R.
   Phenazoni . . . . gr. xx
   Tincturæ gelsemii · . . . . min. xx
   Aquæ chloroformi . . . . . ʒij

Signa.—The draught, one-fourth part for a dose every second or third hour, as required.

Phenazone is not a safe remedy in childhood or in advanced life, or in the weakly. Phenacetin may then be substituted for it. Salicylate of

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[1] That is, whey made by adding one part of buttermilk to two parts of fresh milk, heated to 140° F., in a saucepan.

sodium, in 10-gr. doses, may be given in effervescence with granular effervescent citrate or hydrobromate of caffeine, 1 or 2 drms. in half a tumblerful of water, twice or thrice daily.

In the depression of convalescence, tonics are indicated. One of the best is nux vomica, which may be given in the form of the tincture, in combination with Schacht's solution of bismuth and infusion of calumba. Liquor strychninæ hydrochloratis with dilute phosphoric or hydrochloric acid, and tincture of orange peel, is an excellent " pick-me-up." The dose of the solution of strychnine should not exceed 3 or 5 minims twice or thrice daily, else headache and a feeling of throbbing and fulness may be produced. This mixture may be given in the form of an effervescing draught, citric acid being added to it, and an alkaline mixture of suitable strength being separately prepared. Tincture of lemon may be prescribed instead of tincture of orange peel, if so desired. Strychnine may also be injected hypodermically in like doses to the above. Equal parts of the official liquor strychninæ and distilled water make a suitable solution for hypodermic injection, in 10-minim doses.

Alcoholic stimulants may be required for a short time, especially in the presence of complications; but they should be taken as medicine in specified quantities, and only as ordered by the physician. The mental state of the influenza patient renders alcohol a particularly risky and unreliable remedy; nor should it be forgotten that the abuse of alcohol is a powerful predisponent to influenza, and a prime factor in raising the mortality from it.

J. W. MOORE.

DIPHTHERIA.

Syn., Fr., *Diphthérite*; Ger., *Diphtherie.*

An acute infective disease produced by the invasion of a mucous membrane—usually of the mouth, nose, pharynx, or larynx—or of an open wound, by the *Bacillus diphtheriæ*, which leads to the formation of a false membrane, and elaborates poisons which produce constitutional symptoms, frequently ending in widespread paralysis.

The adoption of the diphtheria bacillus as the criterion by which true diphtheria is to be distinguished from other membranous inflammations, will probably involve some reconsideration and modification of the older clinical view of the disease. For it is no uncommon thing to meet with cases of sore-throat which, though presenting but little, if any, resemblance to the clinical type of diphtheria, have to be included in the category owing to the presence of the diphtheria bacillus; while, conversely, cases exhibiting many of the clinical features of diphtheria must be excluded from the list owing to its absence.

History.—The records from the sixteenth century onwards, though confused by the juxtaposition and intermixture of diphtheria with scarlatina anginosa and other forms of putrid sore-throat, afford reliable descriptions of the disease, which appears to have undergone little, if any, modifications in its general characters. There are good reasons for believing that diphtheria has existed from the earliest times. Excellent accounts of diphtheria in its epidemic form were published by Starr, Huxham, Fothergill, Ramsey, Bard, and others during the latter half of the eighteenth century. During the earlier years of the present century, croup, as it was then styled, occurred mainly in the sporadic form.

It reappeared in epidemic form in Great Britain between 1855 and 1858 as part of a sudden uprising of the malady in many parts of the world. In France the epidemic type asserted itself somewhat earlier (Boulogne sore-throat), and Bretonneau first named the disease diphtheria in his account of epidemics occurring at Tours in 1818–21.

The disease is endemic in many parts of the United Kingdom, both in town and country. It tends to become epidemic at certain seasons. The broad geological features of a district do not appear to influence its prevalence. On the other hand, a damp, exposed site, with a wet surface soil, would seem to favour it. Epidemic prevalence commonly begins in September, reaching its highest point in October or November, and then declines slowly in December and January. At times a small recrudescence is observed in March or April. The fatality of different epidemics varies within wide limits. In some the disease is rarely fatal, whilst in others the constitutional symptoms are severe, and laryngeal and nasal complications are frequent. During the last twenty years there has been a progressive increase in the rate of mortality from diphtheria in England and Wales, and along with this a wider diffusion of the disease, and apparently some shifting of its incidence from rural districts to urban populations. It is worthy of note that this increase coincides, in point of time, with a progressive improvement in sanitary circumstances generally, and with a continuous diminution in the death-rate from most of the other acute infectious diseases (Thorne).

Diphtheria sometimes complicates scarlet fever and measles, and more rarely other infectious diseases. Women and girls are attacked more frequently than boys and men, probably because of their greater opportunities of coming into close contact with the sick, and partly, it may be, on account of the greater prevalence among them of the habit of kissing. During the age period 5–10, girls are one-third more liable than boys.

The influence of age is very marked both as regards attack-rate and mortality. Speaking generally, it may be said that there is a special incidence of diphtheria on the age period 3–12. The fatality of the disease is very high in the first quinquennium of life, and highest of all in infants under 2 years of age. It falls sensibly after the tenth year to rise again after 40. These features of the disease are well illustrated by the accompanying table (Goodall and Washbourn), which shows the numbers and ages of the patients admitted into the hospitals of the Metropolitan Asylums Board during the years 1888 to 1894, with the number of deaths and fatality per cent.:—

Ages.	Number Admitted.	Deaths.	Fatality.
Under 1	199	123	61·8
1 — 2	688	434	63·1
2 — 3	966	532	55·1
3 — 4	1,259	608	48·3
4 — 5	1,323	516	39·0
Total under 5,	4,435	2,213	49·9
5—10	3,723	1,046	28·1
10—15	1,330	141	10·6
15—20	782	34	4·3
20—25	543	25	4·6
25—30	354	19	5·4
30—35	183	9	4·9
35—40	110	5	4·5
40 and upwards,	188	24	17·4
Totals,	11,598	3,516	30·3

Etiology.—**Nature of infection.**—Diphtheria is highly contagious. The contagium (the *Bacillus diphtheriæ*) is usually conveyed out of the body with the pharyngeal, buccal, or nasal secretions.

It does not appear to diffuse itself readily through the air ; at any rate those brought into close contact with the sufferers are the most likely to become infected. Virulent diphtheria bacilli have on many occasions been found in the mouths of healthy individuals, and of persons who, in every other respect, have completely recovered from an attack of diphtheria. The bearing of these observations on the manner in which the disease may spread is obvious. The contagium readily attaches itself to clothes, bedding, etc., and may exhibit considerable vitality outside the body. In one instance within the writer's knowledge, outbreaks of the disease continued to recur at intervals in an hospital ward, in the face of the most stringent precautions, until the old flooring had been entirely removed and replaced by a new one.

Among the children of the poor, the common practice of passing sweets from mouth to mouth affords a ready means of spread. Occasionally the disease is acquired by the direct inoculation of a wound or abrasion, or the poison may be introduced with the food (see Milk infection). Direct infection from person to person is, however, the common way in which diphtheria is communicated.

The question of school influence on the spread of diphtheria has occupied attention for many years. Some of the ways in which it appears to be operative for mischief have been summarised by Thorne as follows :—

" 1. It brings together those members of the community who are, by reason of age, most susceptible to diphtheria.

" 2. The children thus brought together are placed, and remain for many hours of the day, in exceptionally close relation to each other.

" 3. The closer the aggregation and the greater the hindrance to free movement of air, the greater the risk.

" 4. Faulty sanitary conditions of the schoolhouse and its surroundings, and such other conditions as tend towards a state of general ill-health, in so far as they induce sore-throat, favour the reception of any imported diphtheria infection.

" 5. The practices of kissing and of transferring sweetmeats from mouth to mouth,—practised more commonly among girls than boys,—the joint use of drinking cups and the like, must assist in the diffusion of diphtheria amongst school-fellows."

It has been shown in several epidemics of diphtheria, that while the schools remained open, the rate of attack among children between 3 and 12 years of age, who were presumably susceptible to the disease, was from two to four times greater in those attending school than in those remaining at home. More recently, attention has been directed to the sudden drop in the notifications of diphtheria in London during the ordinary late summer holiday period, and to the increase which follows the re-opening of the schools. Shirley Murphy, who drew attention to this phenomenon, attributes it to diminished prevalence at the school age period of life during the holidays. There seems little doubt that school influence must be reckoned a feature of some importance. The data at present available hardly admit of an exact statement being made of the extent to which it is operative in the spread of the disease. It would appear to lie somewhere between 5 and 20 per cent. of the cases occurring during the school age period (3–12 years).

Transmission by milk.—There is evidence that diphtheria may be transmitted by infected milk, and many extensive outbreaks of the disease have been traced to this agency. The sufferers are mostly to be found among the milk consumers in affected households, especially where raw milk is habitually consumed. Stored milk, whether in the form of cream or skim-milk, appears to be more potent for mischief than fresh milk. It has been shown that the diphtheria bacillus will multiply in milk at temperatures of from 64°·4 to 68° F. Exposure of milk, in whatever way, to the contagium of human diphtheria may therefore lead to its infection. According to some observers, the infection in certain outbreaks is derived from the cow. The disease does not appear to be capable of transmission through the agency of drinking water.

Communication by animals.—Cats suffer from a pseudo-membranous infective disease resembling diphtheria, and many instances have been recorded which seem to show that human diphtheria may be derived from a cat so diseased. It has been suggested that the disease in the cat may be contracted in the first instance from a human case, and transmitted from cat to cat. The identity of the two diseases is accepted by some authorities in this country. The so-called diphtheria of fowls is associated with a bacillus which differs in many ways from that of diphtheria. Loir and Duclaux have recorded a case of membranous sore-throat in a child, which occurred during the prevalence of an epidemic of avian "diphtheria." They obtained from the false membrane typical cultures of the bacillus of avian diphtheria, but failed to discover the *Bacillus diphtheriæ*.

Influence of surroundings.—Very little is known at present of the life history of the diphtheria bacillus outside the human body. It is capable of persisting for many weeks in the throats of persons who have recovered from the disease, and may be found in the throat or clothing of those in close attendance on cases of diphtheria, and in the dust of diphtheria wards. It is probable that the diffusion of the virus about cases of diphtheria is considerable. As regards the influence of sanitary circumstances, Thorne makes the following observation: "That the only available vital statistics as to diphtheria do not support the contention that this disease and its increase in this country are related to faulty sanitary circumstances; that much diphtheria which in former times would undoubtedly have been assigned to faulty sanitary circumstances is now found to be communicated to man through the agency of milk; that there are good reasons for believing that sore throats which are induced by exposure to conditions such as drain emanations, render people especially susceptible to the influence of the diphtheria contagion"; and that amongst those attacks "in which there is, in appearance at least, a connection between exposure to foul emanations and diphtheria, some of them may possibly be instances in which a process of development, even in the same person, leads from a minor affection up to a major and definitely specific disease."

Bacteriology.—The bacillus of diphtheria is found in every case of true diphtheria. In length it varies from 2 to 3 μ, and in thickness from 0·5 to 0·8 μ. The bacilli are straight or slightly curved motionless rods, disposed in irregular clusters or in parallel bundles, but never in chains. A long and a short variety are commonly recognised. The short rods are often somewhat thickened at one end, or present a swollen centre tapering towards rounded extremities. Curious club - shaped or pear-

shaped involution forms[1] occur both in cultivations and in false membrane. The bacilli stain readily by Gram's method or with alkaline methylene-blue. The segmented appearance presented by some stained preparations is due to metachromatism. Sporulation does not occur. The Klebs-Löffler bacillus grows readily on serum at 37° C.

The pseudo-diphtheria bacillus (Hofmann's bacillus) is sometimes met with in the throats of patients suffering from true diphtheria. The rods are short, wedge-shaped, and generally united in pairs, with the bases in apposition. The colonies are practically indistinguishable from those of true diphtheria, and old cultivations similarly present clubbed forms. Hofmann's bacilli stain uniformly. They differ in the main from those of true diphtheria in being non-pathogenic to animals. Goodall and Washbourn give the following directions for making a bacteriological examination in cases of suspected diphtheria :—

" The tongue is depressed with a spatula, and a portion of the exudation is removed by scraping or rubbing over the fauces with a sterilised instrument. For this purpose either a platinum rod is employed, which can be sterilised in a flame just before use; or a plug of cotton-wool fixed on the end of a metal rod, previously sterilised, and kept in a sterilised test-tube plugged with cotton-wool. In laryngeal cases, if the fauces are not visibly affected, the instrument must be passed as far as possible downwards towards the larynx. Two or three blood-serum tubes are then inoculated by smearing their surface with the platinum rod or plug of cotton-wool. The tubes are placed in an incubator and kept at the body temperature. At the end of twelve or eighteen hours the diphtheria colonies appear as opaque, white, round masses the size of a pin's head. On microscopical examination, a diagnosis can be made. A portion of one of the colonies is removed with a sterilised platinum wire, is diluted with a drop of water, and spread over the surface of a cover-glass. The cover-glass is allowed to dry in the air, is passed three times through a flame, and is stained for five minutes in a solution of carbolic methylene-blue.[2] The cover-glass is then washed with water, dried in air, mounted on a slide with Canada balsam, and examined with a one-twelfth oil-immersion lens. Should the case be one of diphtheria, bacilli with the characters already mentioned will be found.

" If the exudation on the throat be examined directly under the microscope it will in all cases show a number of different kinds of bacteria. Many of these bacteria are the normal inhabitants of the mouth, and do not form colonies on blood serum. Consequently in some cases of diphtheria the only colonies which develop in the tubes are those of the diphtheria bacillus. But in the majority of cases other colonies also develop. The most important of these are minute transparent colonies of a streptococcus similar to, if not identical with, the streptococcus pyogenes. . . . We must add that a single bacteriological examination will not always detect the presence of diphtheria bacilli, even in cases of undoubted diphtheria. This may be due to the cultivation having been taken from an area free from bacilli, to the local use of antiseptics, or to some error of examination."

In cases of laryngeal diphtheria the bacilli should be sought for in the pharyngeal or faucial—not tonsillar—secretions. As a rule, the bacilli

[1] There is still some difference of opinion as to the nature and significance of these aberrant forms.

[2] Löffler's alkaline methylene-blue solution may also be used with advantage. It is prepared as follows :—Concentrated alcoholic solution of methylene-blue, 30 c.c. ; solution of caustic potash (0·01 per cent.), 100 c.c.

obtained from cultures are somewhat smaller than those obtained directly from false membrane.

Mixed infection is the term applied to cases in which considerable numbers of pyogenic bacteria (streptococci especially) are found associated with the diphtheria bacillus. It is held by some Continental observers that their presence is of unfavourable import, but this view is not supported by observations made in this country. There can be no doubt, however, that these organisms may produce secondary septic complications, and many cases of septic and hæmorrhagic diphtheria are probably largely due to their agency.

Membranous affections resembling diphtheria, at times closely resembling diphtheria clinically, may occur in association with other micro-organisms. This is notably the case in the sore throat of scarlet fever, where streptococci or other pyogenic bacteria are met with. Not infrequently, however, patients suffering from scarlet fever have true diphtheria bacilli in their fauces, and the two diseases may occur simultaneously or consecutively in the same patient.[1]

In many cases of acute follicular tonsillitis, particularly among children, the exclusion of diphtheria can only be made with certainty by bacteriological examination. Membranous affections of the throat have also been described in association with measles, typhoid fever, and whooping-cough, which are not necessarily associated with the diphtheria bacillus. Experience tends to show that these non-diphtherial membranous affections are rarely communicated to others. Their occurrence in the course of the acute specific fevers is often of grave import, and in many cases septicæmia accelerates a fatal issue. Paralysis does not occur.

Morbid anatomy.—With the exception of false membrane, there are few macroscopic changes after death from diphtheria. The position and extent of the membrane naturally varies considerably. It is to be found in most cases on the tonsils and fauces and contiguous mucous membranes, but may be entirely limited to the larynx and air passages, or to the nose. It is often more adherent over the tonsils and pharynx than in other situations. False membrane may occasionally be traced downwards into the smallest bronchi; but more usually after the second or third branchings the membranous structure insensibly passes into a muco-purulent non-adherent material. The consistence of the membrane varies greatly in different cases, peeling off in large flakes in some, whilst in others it is pultaceous or shreddy and friable. In very malignant cases there may be necrosis of the mucous membrane and sloughing of the tonsils and palate. Where the false membrane has separated before death, there is often a granular appearance of the mucous membrane.

Diphtheritic false membrane consists of a fibrinous meshwork enclosing masses of dead epithelium and leucocytes and some red blood cells. The cellular constituents are derived from the superficial layers of the epithelium, together with migrating leucocytes which are destroyed by the poison and with the surrounding elements undergo hyaline transformation

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[1] An examination of 100 consecutive cases sent to the Eastern Hospital certified to have scarlet fever showed the following results (Goodall): eighty-seven had scarlet fever, and in six of these there were diphtheria bacilli of the long variety. In thirteen cases the short variety only of the bacillus, or organisms indistinguishable from it, were found. Of the thirteen other cases, two were cases of diphtheria, five were cases of rötheln, in one of which the short variety of the diphtheria bacillus was found; three were cases of measles, one a case of pneumonia with the short variety of the diphtheria bacillus, one a case of diarrhœa, and one a case of tuberculous meningitis.

(coagulation-necrosis of Weigert). The subjacent epithelium is usually destroyed, and no definite line of demarcation can be made out between it and the false membrane. The deeper layers of the mucous membrane may be infiltrated with fibrin and leucocytes, and may exhibit areas of hyaline transformation. The formation of these foci of necrobiosis, starting from the epithelium and proceeding inward, is, according to Oertel, the distinguishing characteristic of diphtheria. The diphtheria bacilli are generally found at or near the surface of the false membrane, and in some cases they have been obtained, after death, from the spleen, kidneys, and lymphatic glands. In cases complicated by streptococcus infection, these organisms may be found in the mucous membrane and in septicæmic lesions of the internal organs.

The visceral and other changes met with are variable. In laryngeal cases areas of collapse, which are often extensive, and patches of lobular pneumonia are usually present in the lungs. Diphtheria bacilli can often be cultivated from the alveolar contents in such cases. Accumulation of muco-pus in the bronchi is often met with, especially after tracheotomy. Wholesale collapse of the lung, sometimes affecting an entire lobe, is a common event in cases in which the diaphragm or intercostal muscles have been profoundly paralysed. The right lower lobe appears more liable to be affected in this way than any other part of the lungs. The cervical and submaxillary glands are nearly always swollen and firm on section. The bronchial glands are similarly affected where there have been pulmonary complications. Foci of suppuration in the lymphatic glands are very exceptional. Swelling of the solitary glands of the intestine and of Peyer's patches is frequently well marked, but ulceration does not occur. In such cases the mesenteric glands are also enlarged. The spleen is generally somewhat enlarged and firm. Cloudy swelling of the spleen, liver, and kidneys is usually present. The kidneys may appear quite normal even where there has been albuminuria, or may exhibit varying degrees of parenchymatous inflammation, especially where signs of acute nephritis or suppression of urine have been present.

The right cavities of the heart often contain a considerable quantity of decolorised clot, more or less adherent according to the slowness with which death has taken place. Inflammation of the endocardium is hardly ever met with. Pericarditis is equally rare. Granular or fatty changes in the myocardium are by no means uncommon, and are present in most cases where death was due to cardiac failure. Cardiac syncope has been attributed by some observers to an interstitial myocarditis. When death occurs at a later stage, in the course of a multiple paralysis, the heart presents the appearances usually found in death from asphyxia. The right cavities are distended with blood and black clot, and subpericardial and subpleural ecchymoses are not uncommon. There may be myocardial changes, but the symptoms point rather to a lesion of the cardiac nerves as the cause of heart failure in these cases.

Degenerative changes have been found both in the medulla and spinal cord and in the peripheral nerves. The prevailing opinion is that the latter is the chief, and often the only cause of the paralysis. The affected nerves do not degenerate in their whole extent. In the affected segments the white substance of Schwann is broken up and attenuated. The axis cylinder may remain intact, or become ruptured, whilst the primitive sheath remains unaffected. There is no interstitial change. It is a degeneration of the nerve fibre itself (Sidney Martin). Similar changes

occur in the sensory and sympathetic nerves. On the other hand, a true interstitial neuritis may affect the nerves of the palate.

Hæmorrhages are usually met with in cases of extreme malignancy. On the surface they occur in the form of petechiæ or ecchymoses, and internally are chiefly met with in the serous membranes, loose areolar tissues, muscles, and alimentary canal.

Symptomatology.—Diphtheria is at the outset a local affection. The constitutional symptoms are due to the absorption into the system of soluble poisons produced by the bacilli at the seat of the local disease. The severity of the constitutional symptoms is proportional to the degree of infection; *i.e.* to the dose of poison absorbed from the primary lesion. Speaking generally, there is a correspondence between the extent of the local affection and the severity of the general symptoms. The term *simple* or *benign* is applied to cases in which the general disturbance is slight, the term *malignant* to those in which the toxæmia is profound.

Incubation. — This is always short; often two days, sometimes three or four, probably never exceeding seven.

Invasion.—This is often unobtrusive or insidious, but a sudden onset, with or without rigor or chills, is not uncommon. The early symptoms are mainly those of fever—chilliness, headache, shifting pains in back and limbs, nausea, and general malaise. In infants the onset may be heralded by convulsions and vomiting. Sore-throat may be complained of, but is often very slight or absent at first. In infants difficulty in swallowing or disinclination for food are of common occurrence.

Course. — It will be convenient to begin with a description of the symptoms of an ordinary uncomplicated case of faucial diphtheria. The initial rise of temperature is generally moderate; 100°–102° F., sometimes higher. The fauces are usually swollen and dusky red, though occasionally pale and glistening before the appearance of membrane. The breathing is somewhat hurried, and the pulse rate increased. The urine presents the usual febrile characters, and may contain a trace of albumin.

The development of the disease is rapid. Within a few hours of the onset there may already be indications of false membrane in the shape of one or more whitish specks or patches on the tonsils or fauces. At this stage the appearance of the throat may closely resemble that of acute follicular tonsillitis. Sometimes the appearance of the exudation is delayed for several days, and rarely the local inflammation is unaccompanied by membrane. In the majority of cases false membrane is already present when the patient first comes under observation. The patches of false membrane, which may be ill-defined at first, soon increase in size and consistency, and may extend so rapidly as to cover the whole of the fauces and pharynx within forty-eight hours. There is generally considerable œdema of the affected area, so that on looking into the mouth the opening of the fauces is more or less obliterated. The colour and consistency of the false membrane vary considerably. At first it is whitish or yellowish white, of varying opacity, and somewhat loosely adherent; as it increases in thickness and extent, it tends to become more yellow or even brown and leathery, and can only be removed with some difficulty, leaving a raw-looking surface with bleeding points. New membrane rapidly takes the place of that which has been removed. There is generally more or less mucous exudation and accumulation about the fauces, and sometimes signs of coryza and a thin acrid discharge from the nostrils. As the local lesion extends, the general symptoms increase in severity, and throat

symptoms become more prominent. Anæmia and bodily weakness become marked, and in severe cases the surface may present a dusky hue. The glands at the angles of the jaws and their lymphatic connections become swollen, painful, and tender. The pulse is frequent, small, and compressible. The tongue is thickly furred on the dorsum, and tends to become dry. Appetite quickly fails, but is seldom totally lost. Mastication and swallowing may be difficult and painful, though rarely to the same extent as in acute follicular tonsillitis. The temperature ranges irregularly between 100° and 102°, but may occasionally reach 103° or even higher. In an uncomplicated case the chest will reveal nothing on examination, unless it be scanty signs of bronchial catarrh. In a large proportion of cases the urine contains albumin. In a favourable case the symptoms may begin to subside as early as the fourth or fifth day, more often at the end of a week or ten days. The membrane ceases to spread, and is thrown off in flakes or shreds and does not re-form. The swelling of the neck subsides, and convalescence begins.

Varieties.—Deviations from this favourable course are frequent, and are due partly to extension of the local disease in various directions, partly to the degree of systemic infection.

Benign diphtheria has usually limited local disease, and the constitutional symptoms are very mild and indefinite. Fever is slight or absent; slight soreness of throat on swallowing may be complained of for a day or two, and on examination one or two loosely adhering patches of membrane may be seen on the tonsils, though they may already have disappeared when the patient comes under observation. Anæmia and debility are nearly always present, and may be the most striking features of the illness. Some enlargement of the cervical glands is also common. There can be no doubt that many cases of this nature escape notice altogether, and may be important factors in spreading the disease. It is further to be observed that the mildness of the primary disease does not exempt the patient from the risk of complications or dangerous sequelæ. Exceptionally there may be extensive local disease with very slight constitutional disturbance.

Malignant diphtheria is characterised by severity rather of the constitutional symptoms than of the local lesions. The virulence of the attack may manifest itself from the outset, but severe systemic symptoms commonly make their appearance somewhat later. Prostration is extreme, the surface often dusky or ashen grey, the pulse rapid and feeble, the tongue dry, the fever often high, though occasionally the temperature may be normal or even subnormal. The urine is albuminous, but very rarely bloody. Erythematous or petechial eruptions are not uncommon, and there may be bleeding from the mucous membranes and into the cellular tissues (hæmorrhagic diphtheria). Extension of the inflammation to the nose is a common feature of malignant diphtheria. Throat symptoms, however, are not necessarily prominent. Even in the most malignant form of the disease, which kills by intense toxæmia, the appearances may differ but little from those presented by a case of ordinary severity. Sometimes the membrane becomes dark and pultaceous from decomposition, and imparts an offensive odour to the breath. This condition has been mistaken for gangrene. In other cases, very great swelling of the fauces and underlying tissues is associated with a thin and ill-defined exudation. Extension of the local inflammation to the deeper structures is usually attended by marked swelling of the cervical glands and connective tissues,

and at times the whole neck becomes deformed by diffuse brawny swelling from the jaw to the collar bones. Gangrene and deep ulceration at the mucous surface, extravasations of blood, and suppuration in the deeper tissues of the neck, are all of rare occurrence. The heart usually fails rapidly, and in most cases death by asthenia takes place within a short time, or quite suddenly from syncope.

Extension of false membrane. — This may take place in several directions:—(*a*) Into the larynx and trachea; (*b*) into the nasal cavities, along the lachrymal ducts or into the Eustachian tubes; (*c*) into the œsophagus; and (*d*) to other mucous membranes, or to wounds or excoriations.

Laryngeal diphtheria.—The formation of false membrane in the larynx gives rise to one of the most common as well as one of the most fatal varieties of the disease. It occurs mainly, though not exclusively, among children. The laryngeal affection is either primary (diphtheritic or membranous croup), in which case laryngeal symptoms predominate from the outset; or more commonly it is due to extension of the local inflammation from the fauces or pharynx, such extension generally taking place between the third and sixth days of the disease. The symptoms are characteristic and unmistakable. Some hoarseness of voice and a dry, short, sometimes metallic, cough are among the earliest indications. Very soon attacks of paroxysmal dyspnœa supervene with noisy stridor, especially during inspiration. At first these attacks may be separated by considerable intervals, during which the child exhibits but few signs of distress, and in favourable cases the laryngeal symptoms often subside after a few paroxysms of moderate severity. In bad cases the attacks increase in frequency and violence, and before long the dyspnœa becomes continuous. Huskiness gives place to complete aphonia, the face and extremities become livid, and the pulse more frequent and small. There is extreme restlessness, and a look of intense anxiety on the face as the child clutches wildly at its throat or at anything within reach in its vain attempts to get breath. The respiratory movements are violent, though ineffectual; there is marked inspiratory recession at the epigastrium and above the clavicles. As suffocation advances cyanosis deepens, the face and extremities become cold and clammy, and the patient gradually passes into a semi-comatose condition, death eventually taking place by asphyxia. The suffocative phenomena in this form of the disease are mainly due to the occlusion of the larynx by false membrane, and may be temporarily relieved by the expulsion of pieces of membrane or plugs of mucus through the mouth.

In children death sometimes occurs within a few hours of the onset of laryngeal symptoms, not often later than the fifth day. In adults the course of the disease is usually less acute. The onset of inspiratory dyspnœa is gradual, and the paroxysms when they occur are far less distressing. Prostration is usually well marked, but dyspnœa may not become obtrusive until the membrane has reached the smaller bronchial tubes.

In cases where laryngeal dyspnœa has been relieved by tracheotomy, pulmonary dyspnœa may ensue from several causes, of which the chief are—(1) Extension of membrane downwards into the smaller bronchi, a condition frequently associated with broncho-pneumonia; (2) congestion of the lungs; (3) collapse of the lungs; (4) acute insufflation of the anterior part of the lungs. The auscultatory signs in laryngeal cases are very variable. Loud laryngeal stridor is often audible over the lungs during the paroxysms, the vesicular sound being very faint or entirely obscured. The

extension of membrane into the bronchi may be very difficult to recognise during life. In protracted cases there may be signs of broncho-pneumonia, but more often increasing lividity and asthenia, excessive inspiratory recession of the lower thoracic zone, with diminished or suppressed auscultatory phenomena, afford the only indications. Subcutaneous emphysema of the neck and chest is occasionally met with.

Nasal diphtheria.—The nose is usually invaded by extension from the pharynx, but is also occasionally the seat of the primary infection. The prominent symptoms are blocking of the nares, and a thick muco-purulent or thin sanious irritating discharge from the nostrils. Respiration is usually embarrassed, and often snuffling. Epistaxis occurs frequently, and may be severe. False membrane may be visible within the nostrils, but is more often limited to the back of the nasal cavities. Very exceptionally it spreads from the nostril over the excoriated upper lip. Glandular swelling is usually well marked. The inflammation may extend into the lachrymal ducts, and infection may possibly reach the conjunctivæ through this channel. There is often associated faucial or pharyngeal disease. The constitutional symptoms are usually severe. The frequency of nasal complications in malignant diphtheria has already been alluded to.

Reference may here be made to a remarkable affection described by American observers. It consists of a membranous or fibrinous rhinitis, occurring usually in children, and running a benign course with little or no constitutional disturbance. The nares are occupied by thick membranes, which rarely extend beyond the nose; and a large majority of the cases examined yield the *Klebs-Löffler bacillus.* Infection of other children in the same family is rare. Otitis media may be caused by extension along the Eustachian tubes, and rarely the external auditory meatus becomes invaded through a ruptured tympanic membrane.

Œsophageal diphtheria.—The spread of false membrane along the œsophagus, and even into the stomach, is seldom recognised during life. It is altogether of rare occurrence, and does not give rise to any special symptoms.

Irregular diphtheria.—External wounds and abrasions may become secondarily affected in persons suffering from diphtheria. But cases occur, on the other hand, in which a wound is the site of the primary disease, which is followed in due course by general infection. In rare instances the primary lesion is situated on the female genital organs, or about the anus. It should be noted in this connection that pseudo-membranous inflammation of wounds and ulcerated surfaces may also be due to streptococcus infection. A granulating wound is very seldom affected by the *Bacillus diphtheriæ,* and though the tracheotomy wound may become foul, true diphtheritic membrane is very rarely found upon it.

The term latent diphtheria has been applied to cases in which faucial or pharyngeal inflammation, due to the bacillus diphtheriæ, is not accompanied by pellicular exudation, and to cases of nasal and laryngeal diphtheria in which an exact diagnosis is not arrived at.

Prolonged form of diphtheria.—Cases have been recorded by several observers in which diphtheritic membrane continually re-formed for many weeks, and even months. The mucous membrane of the nose appears to be specially susceptible to this form of the disease. Death sometimes occurs, chiefly from laryngeal complications.

Protection.—Although an attack of diphtheria does not protect against recurrence of the disease, the writer is inclined to agree with those who

hold that one attack confers some degree of protection. As a rule, second attacks are not so severe and dangerous. To this rule, however, there are exceptions.

Relapses.—Though recrudescence of the sore throat is not uncommon, true relapses—supervening before the patient has completely recovered from the effects of the primary attacks—are comparatively rare. Goodall and Washbourn met with them in 16 out of 1071 consecutive cases of diphtheria admitted into the Eastern Hospital.

Analysis of symptoms.—One or two features of the disease which have already been incidentally alluded to require somewhat fuller consideration. The temperature is always irregular and rarely high, except occasionally at the onset. It is in no way a characteristic feature of the disease, and does not afford reliable indications of the severity of the case. While it may never rise above the normal in a malignant case, a comparatively mild uncomplicated attack may be ushered in by a temperature of 104° or 105° F. Unusually high temperatures occasionally accompany laryngeal and pulmonary complications.

The enfeeblement of the heart and circulation, which is always met with in diphtheria, is part of the rapid general bodily exhaustion which characterises the disease. The pulse is frequent, of low tension, and may present irregularities of force and rhythm, which are not necessarily of serious import. The heart sounds are weak, and the first sound often short. In rare instances there is extreme slowness of pulse, often associated with anuria and vomiting; these cases are almost invariably fatal.

The urine contains albumin in so many cases that this should be looked upon as a symptom rather than a complication of the disease. It probably occurs in from one-half to three-quarters of all cases. Albumin very seldom makes its first appearance after the tenth day of the disease. It may be present on the first day, but is more often found on the third or fourth. The quantity varies considerably in different cases, and often in the same case from day to day. Speaking generally, the amount of albumin is not a trustworthy prognostic sign, though it as a rule appears earlier, and is more copious and persistent in a severe case than in a mild one. It should be remembered, however, that some fatal cases have never had albuminuria, and conversely, that a highly albuminous urine is not a bar to recovery. Œdema is extremely rare. In the large majority of cases, the albuminuria completely disappears within a few days or weeks. The microscopical examination of the urine is often negative in its results; occasionally a few hyaline casts or renal cells may be detected.

Vomiting, especially repeated vomiting, is, in the writer's experience, an almost invariably unfavourable symptom, whether it occurs during the height of the disease, in association with anuria, or heart failure, or during the cardio-pulmonary crisis of a multiple neuritis.

Complications and sequelæ.—*Heart failure* may occur at any stage of the acute disease, or at a later period in association with other paralyses. More rarely it takes place during convalescence from the primary disease. Early or primary cardiac failure is generally associated with varying degrees of fatty degeneration of the myocardium, apparently the result of a direct action of the poison on the heart itself. It is to be distinguished, clinically at least, from the feebleness of the circulation which occurs in most cases of diphtheria as part of the general bodily prostration. When cardiac failure is gradual, the indications are usually definite. The pulse

rapidly loses strength, and the heart sounds, the first especially, become very feeble or inaudible. The frequency of the pulse may be increased or diminished, or there may be marked irregularity. Cardiac distress and dyspnœa are often experienced, particularly by older patients. Extreme pallor of the face and profound prostration are usually striking symptoms. The body temperature falls continuously, and the extremities quickly grow cold and moist. Consciousness is retained to the end, which may be delayed for several days. In some cases, fatal syncope takes place absolutely suddenly, without warning of any kind; but more usually life is prolonged for some hours. Heart failure, occurring in the later stages of the disease, will be dealt with under the head of paralysis.

Lobular pneumonia is a frequent and very grave complication of diphtheria of the air passages. Its occurrence is usually attended by rise of temperature,—sometimes to a great height,—increased rapidity of breathing, and at times by signs of patchy consolidation of the lungs.

Paralysis.—The frequency of this sequela has been variously stated at from 10 to 25 per cent. of the cases which recover from the primary disease. The period of onset is uncertain. Not infrequently a careful examination will reveal sluggish action of the pupils, or loss of power of accommodation for near objects, even before the beginning of convalescence after the primary disease. More often, however, there is a varying interval between the cessation of the primary attack and the recognition of the signs of paralysis.

According to some observers, the liability to paralysis appears to diminish somewhat with age, but others hold the contrary opinion. The comparative infrequency of paralysis after laryngeal diphtheria is doubtless in part due to the high fatality of this form of the disease. The degree of paralysis does not appear to be in any way related to the severity of the primary disease. Paralytic symptoms are apt to develop earlier after a severe attack; but some of the worst cases are met with after mild attacks of the primary disease. Occasionally the appearance of paralysis is the first indication of a previous attack of diphtheria. The symptoms necessarily vary widely, according to the nerves affected.

The onset is for the most part gradual, and the paralysis at first limited in distribution. It may remain more or less localised throughout the attack, or become generalised.

Paralysis of the palate is very common, and usually the earliest to appear. It either occurs as a local effect of the inflammatory changes of the primary disease on the muscles and nerves of the palate, or develops as a consequence of the parenchymatous degeneration of the peripheral nerves, which is the chief cause of the paralytic phenomena of diphtheria. On inspection, the velum palati is seen to hang motionless during respiration and phonation, and is insensitive to touch. The paralysis may be unequally developed on the two sides, and in very rare instances is unilateral. Paralysis of the palate is characterised by a peculiar nasal quality of the voice, and a tendency to the regurgitation of fluids through the nose during the act of swallowing, owing to the impossibility of shutting off the posterior nares from the general cavity of the pharynx. Associated difficulty in swallowing from paralysis of the pharynx is frequent. In many cases the paralytic symptoms do not proceed beyond this, and the affected parts recover completely after a varying interval. Frequently, however, other parts of the body become affected. Paralysis of the ocular muscles is not uncommon. Affection of the ciliary muscle entails loss of

power of accommodation, for near objects especially, and a sluggish reaction of the pupils to light. Internal squint is comparatively frequent, ptosis much rarer. The writer has seen one patient with complete ophthalmoplegia of both eyes, but such cases are altogether exceptional. Concentric contraction of the fields of vision and temporary amaurosis have also been described, but changes in the fundus oculi do not take place. Deafness and loss of taste and smell are very rare manifestations. Headache does not occur. Facial paralysis occurs rarely, and is ill-defined.

Paralysis of the limbs is not infrequently the first symptom to draw attention to the condition of the patient, and is met with in every degree of severity. Tingling and "pins and needles" sensations may be complained of by older children and adults in the parts about to become paralysed. The affection of the limbs is usually bilateral, and the legs commonly suffer before the arms. There is nearly always more or less ataxia and unsteadiness of gait, very marked indeed in some cases. As the paralysis increases, the limbs gradually become quite useless, and the affected muscles waste visibly. Muscular power, however, is rarely completely abolished. Faradic irritability is gradually extinguished, but the galvanic reactions are usually retained. Disorders of sensation are not uncommon, and occasionally some anæsthesia of the extremities can be made out. The condition of the reflexes is variable. The plantar and cremasteric reflexes, though sometimes absent, are for the most part present. The knee-jerks are lost; but before their extinction a period of exaggeration is by no means rare. In some instances an increase of tendon reflexes in the upper limbs has been noticed. Absence of knee-jerks, without palsy, may also be met with either during or after an attack of diphtheria. Recovery of power and of normal electrical reactions is always complete, but may be delayed for several months. In like manner, the date of reappearance of the knee-jerk varies within wide limits.

In cases where the paralysis becomes widespread, the muscles of the back and neck may be affected. It is especially in this class of case that paralysis of the larynx and of the muscles of respiration are prone to develop. The cardio-pulmonary seizures which constitute the gravest danger of diphtheritic multiple paralysis are, in the writer's experience, usually confined to cases of this type. The general symptoms and appearance of these patients are sufficiently definite to merit description. They present few, if any, signs of distress as they lie more or less helpless in bed, for the most part on their back. The breathing is quiet, and at times rather slow; it may be sighing in character, but is rarely laboured. The face is pale, at times a trifle dusky, and one is forcibly struck by the listless or apathetic condition of the patients. They instinctively shun any kind of exertion. They are with difficulty induced to speak, and only answer in a whisper, or by a nod of the head. It is the rarest event to hear one cry. They are generally fairly well nourished, and take food readily; but swallowing is often accompanied by a good deal of spluttering and regurgitation through the nose. There is almost invariably paralysis of the palate and pharynx. Laryngeal paralysis is often present. The extremities are always paralysed, and weakness of the muscles of the back and neck is frequently associated. The heart is usually acting weakly, and the movements of respiration are feeble. The bowels act sluggishly; but further than this, disordered action of the sphincters is very rare.

Evidence of paralysis of the larynx is to be found in huskiness or aphonia, and in a characteristic alteration of the cough, which becomes

non-explosive and ineffectual; this change is sensibly accentuated where paralysis of the diaphragm is superadded. Swallowing, especially of liquids, sets up violent and exhausting attacks of coughing and choking, particularly when the mucous membrane is insensitive, and the lower portion of the pharynx and the muscles closing the upper orifice of the larynx are also paralysed. Mucus tends to accumulate in the lungs, and broncho-pneumonia may result from the passage of food particles into the bronchi.

Paralysis of the intercostal muscles is comparatively rare, and may be unilateral. The respiratory movements of the affected region are diminished or lost; and if the paralysis is prolonged, collapse of the subjacent lung is apt to occur, and may give rise to definite physical signs. Paralysis of the diaphragm is of more common occurrence, and of serious import owing to its frequent association with grave symptoms of heart failure (cardio-pulmonary seizures or crises). Diaphragmatic paralysis was met with by the writer in twenty-eight out of sixty-four consecutive cases of diphtheritic paralysis admitted to the North-Eastern Children's Hospital. In seventeen of these cardiac crises occurred. The affection of the diaphragm may come on insidiously, and without obvious symptoms, or develop quite suddenly as part of a cardio-pulmonary crisis.

The cardio-pulmonary seizures are alarmingly sudden in onset. The dominant symptoms are those of asphyxia, with failure of the heart. Vomiting is a common initial symptom. There is urgent dyspnœa, with cyanosis or dusky pallor and extreme restlessness. Inspiration is sighing or gasping, and expiration feeble. The surface and extremities grow cold and clammy. Mucus accumulates rapidly in the air passages, and the lungs become œdematous. When the diaphragm is paralysed, there is usually extensive collapse of the pulmonary bases, which may give rise to physical signs. The pulse becomes very frequent, and arterial tension very low. Irregularity is often present. The seizures vary much in duration and severity. Recovery is rare (five cases out of twenty-two in the series quoted above).

Cerebral complications.—Paralysis of a hemiplegic type is occasionally met with in diphtheria. It may be due to cerebral hæmorrhage, or to thrombosis, or embolism of the cerebral vessels. The onset may be convulsive.

Renal complications.—Suppression of urine is a somewhat rare and almost invariably fatal complication of diphtheria. Its chief features are well illustrated by the following case:—" A girl æt. 3 years was admitted to hospital under the writer's care on 31st March, on the seventh day of the disease. The right tonsil was partly covered by membrane. The child was unusually pale, and very quiet and drowsy. The pulse was regular and small, 48 to the minute. There was frequent and uncontrollable vomiting. During the first twenty-four hours she passed a few drachms of urine loaded with albumin; after this there was total suppression till death on 4th April. There was no œdema. The pulse ranged between 40 and 48. The vomiting subsided after the first forty-eight hours. The heart grew steadily weaker. Death was ushered in by a general convulsion. The kidneys were large and congested, and exhibited, under the microscope, well-marked signs of early tubular nephritis. A sister had died a few days before, also from anuria." In some cases the pulse is frequent and irregular.

Although in most cases albuminuria is symptomatic and rapidly

disappears with convalescence, the condition of the urine is sometimes indicative of nephritis. The total quantity is small, and it contains a large amount of albumin and numerous epithelial or, more rarely, blood casts. Dropsy, however, is extremely rare. This complication is always a grave one. It may pass into complete suppression, and there is reason to believe that it is occasionally the starting-point of chronic renal trouble.

Diagnosis.—It may be laid down as a guiding rule, that in all—and particularly in doubtful—cases of diphtheria a bacteriological examination should, if possible, be made at the earliest opportunity. In any case it is a good rule to "regard as suspicious all forms of throat affections in children, and carry out measures of isolation and disinfection" (Osler).

Faucial diphtheria.—In cases where diphtheria of the fauces is unattended by membranous exudation, the appearances may be indistinguishable from those of simple or catarrhal sore-throat, and a bacteriological examination alone can determine the true nature of the case. The presence of albuminuria in such cases is always suspicious, and the association of laryngeal stridor or of a sanious nasal discharge goes far to establish the diagnosis of diphtheria.

The distinction between diphtheria—at an early stage—and follicular tonsillitis may present considerable difficulty. This is especially the case where the yellow follicular contents escape on to the surface of the tonsils so as to form small patches, or where diphtheria is at first localised in and around the tonsillar crypts. The membrane in the diphtheritic cases generally spreads rapidly to contiguous parts, and the occurrence of other signs of diphtheria will often help the diagnosis. Albuminuria is uncommon in non-diphtheritic inflammations of the fauces, and does not occur in simple follicular tonsillitis. In this affection, too, the phenomena of onset are usually more definite, and labial herpes is not uncommon. Whitish patches, not unlike the false membrane of diphtheria, may be caused by vesicants and escharotics, and by closely set herpes vesicles. The history of the case, and possibly the presence of herpetic vesicles on the lips or face, will reveal the true nature of the faucial affection.

The milk-white spots of thrush (oïdium albicans) may run together to form patches of considerable extent. Their colour is whiter than that of diphtheritic false membrane, and the microscopical appearance of the fungus is unmistakable. Thrush does not give rise to any general symptoms, and is usually met with in marasmic children or in adults suffering from chronic wasting diseases.

In the early stages of scarlet fever, in the absence of rash, the diagnosis from diphtheria may be attended with much difficulty, both in cases where there is exudation on the fauces and where it is absent. Goodall and Washbourn lay stress on the following points: "In scarlet fever the febrile symptoms are more pronounced than in diphtheria, so that a high temperature, a very frequent pulse, and delirium are in favour of this disease rather than diphtheria. Membranous sore-throat with little or no pyrexia is almost certainly diphtheria. Vomiting is much more constantly a prodromal symptom of scarlet fever than diphtheria. Much œdema of the parts underlying the membrane is in favour of scarlet fever, so also is a very red hue of the fauces.

"In cases where the exudation is pultaceous and not distinctly membranous, scarlet fever must be suspected, if the febrile and other symptoms that have just been mentioned are marked. The 'strawberry' tongue is seen more often in scarlet fever than in diphtheria, in which

disease, as in others also, it is occasionally met with; much more character-istic of scarlet fever is the 'peeling tongue.'

"The occurrence of ulceration (unless it be very superficial) and gan-grene of the fauces is exceptional in diphtheria. . . . In all cases, any history of exposure to the specific infection of scarlet fever or diphtheria, as the case may be, is important."

The occurrence of paralysis after an attack of sore-throat may be looked upon as conclusive evidence of its diphtheritic nature. It must suffice to mention that syphilitic and tuberculous affections of the fauces may superficially resemble diphtheria, and to recall the rare occurrence of membranous affections of the same region in enteric fever and other acute specific diseases.

Laryngeal diphtheria.—In the absence of signs of diphtheria in the fauces or elsewhere, this form of the disease in children may be impossible to distinguish from simple or catarrhal laryngitis during life. A case of simple laryngitis usually improves rapidly when placed under favourable conditions, whereas diphtheria tends to grow steadily worse. The catarrhal croup which sometimes accompanies the onset of measles, usually subsides with the appearance of the rash. "The respiratory stridor in some cases of catarrhal croup is excessive, and reaches a height of noisiness which is uncommon in diphtheritic croup" (Gee).

In adults the diseases most likely to simulate diphtheria are various forms of laryngeal ulceration, of growths, œdema of the glottis, and paralysis of the abductors of the vocal cords of sudden onset. A remarkable example of the latter affection came recently under the writer's notice. The patient, a young man, was suddenly seized with laryngeal dyspnœa and cyanosis, which rapidly grew worse and ended fatally within a few days, without any other symptoms declaring themselves. It was most difficult to exclude diphtheria during life.

Prognosis.—The fatality of the disease is very high, ranging in hospital practice (since the introduction of antitoxine treatment), from 18 to 40 per cent. The chief prognostic signs have already been mentioned in the preceding pages, and need only be recapitulated here. Among the chief indications of severity are dusky pallor and extreme prostration, a large extent of membrane, feebleness of circulation, with frequent or unduly slow pulse, early absence of knee-jerk, highly albuminous or scanty urine, epistaxis or other hæmorrhages, extensive glandular swelling and brawny induration of the neck. Repeated vomiting and diarrhœa are both symptoms of ill omen, and convulsions are nearly always of the gravest import. The occurrence of laryngeal complications is most unfavourable. Symptoms of cardiac failure may develop at almost any period of the attack, and in common with widespread paralysis may arise in cases which appeared mild at the outset.

The prognosis in cases of widespread paralysis is always serious and very grave if the muscles of respiration are involved. Recovery from cardio-pulmonary seizures is rare (*vide supra*, p. 211). Death during the course of the primary disease is usually due to one of the following causes:—(1) Suffocation from laryngeal obstruction; (2) pulmonary complications; (3) intense toxæmia; (4) suppression of urine, with or without con-vulsions; (5) heart failure. Death during the course of paralysis is always accompanied by symptoms of heart failure. In most cases there is associated paralysis of the muscles of respiration, especially the diaphragm, with post-mortem signs of asphyxia. Convalescence is often tedious, even

after a mild attack, and complete recovery may be delayed for several months, especially after paralysis.

Treatment.—It will be convenient to consider preventive and remedial measures separately.

Prophylaxis.—The essential points to be attended to in the treatment of every case of diphtheria, however mild, are careful isolation and disinfection. In families or schools where the disease has broken out, every member should be kept under close observation, and suspected cases at once isolated. One chief danger of spread is due to the non-recognition of mild (ambulatory) cases. Another point of great importance is to ensure that the throat is entirely free of diphtheria bacilli before convalescents are sent home. There is abundant evidence to show that virulent bacilli may persist in the throat for weeks or even months after all local signs of disease have disappeared, and become the means of communicating the disease to others.

The *sick-room* should be well ventilated, and free from superfluous hangings and furniture. All discharges from the patient should be carefully disinfected. Pieces of rag should be used instead of handkerchiefs, and immediately burned.

Local treatment should be actively employed in all cases, and in such a way as to avoid mechanical injury of the tissues. The application may be made either with a swab of cotton-wool or in the form of spray, gargle, or by irrigation. In infants this procedure is often most difficult and trying to carry out. Gargles of permanganate of potash or chlorine water may be employed in mild cases. Sprays of perchloride of mercury (1 in 1000 or 2000 parts of water) or carbolic acid (3 per cent. in 30 per cent. alcohol solution) are among the best. They should be used every four hours in mild cases, but more frequently in severe ones. Saturated solutions of boric acid and of bicarbonate of soda are also useful. Irrigation with solutions of boric acid, chlorine, or permanganate of potash is highly spoken of, especially for the treatment of septic conditions of the throat. In nasal diphtheria the nostrils should be kept thoroughly cleansed by syringing or irrigating with dilute disinfectant solutions. If signs of laryngeal affection occur, a steam tent should be arranged upon the bed. Symptoms of croup will often be relieved in this way. Much relief is also sometimes given by a hot bath. If the signs of laryngeal obstruction increase in severity, tracheotomy or intubation should be performed without delay, especially where dyspnœa is urgent and the patient is becoming cyanosed or drowsy. The prospects of success are better in early than in late interference, although it should be added that it is never too late to operate. Of the two operations, tracheotomy is to be preferred. In all cases of tracheotomy it is desirable that the after-treatment should be carried out by properly trained nurses.

General treatment.—The patient should be kept in bed and disturbed as little as possible, on account of the liability to heart failure. The strength should be supported by careful feeding and stimulants. The diet should consist mainly of milk, with small quantities of beef-tea and beef-juices. Alcohol should be given at the first indication of heart failure, and from the outset if the constitutional symptoms are severe. Among drugs, strychnine is perhaps the best. It may be given alone, or in combination with iron. In the treatment of heart failure strychnine is better than digitalis, which is of doubtful efficacy. It is most conveniently administered hypodermically in doses of $\frac{1}{100}$ grain at intervals of three

or four hours. Drugs are of very little use in the treatment of repeated vomiting. Food by the mouth may be withheld, and nutrient enemata or suppositories substituted.

The treatment of paralysis requires rest in bed. When the paralysis remains limited to the palate or ocular muscles, the patient may be allowed to get up at the end of two or three weeks. In cases where it becomes widespread, or in which there is cardiac irregularity, prolonged rest is essential, and it is imperative that the patient should avoid every kind of exertion. Difficulty in swallowing, or evidence of the passage of food into the larynx, should at once be met by giving the food through an œsophageal or nasal tube. The latter is preferable in the case of very young children.

The treatment of the late cardio-pulmonary seizures is almost hopeless. Hypodermic injections of strychnine and brandy should be given, and oxygen inhalations administered. Artificial respiration often causes a temporary improvement, and in two or three cases under the writer's care appeared to contribute towards recovery. Favourable results have also been claimed for tincture of belladonna given in full doses. Galvanism has been recommended for the treatment of paralysis of the diaphragm. Here also the systematic performance of artificial respiration at intervals of a few hours is worthy of trial, with the object of preventing collapse of the pulmonary bases. In the treatment of chronic cases of paralysis of the limbs and trunk, massage and galvano-faradism are useful adjuncts.

Antitoxine treatment.—This consists in the subcutaneous injection of the blood serum of animals rendered artificially immune against diphtheria. The serum used is that of horses that have been immunised by repeated injections of the diphtheria toxine or of cultivations of the diphtheria bacillus. The strength of a serum is gauged by determining how many "normal units" a certain amount contains. A "normal unit" is ten times the amount of serum required to neutralise ten lethal doses of the toxine when injected into a guinea-pig of about 300 grms. The serum acts in two ways upon animals: in minimal doses it renders the animal immune to subsequent injection either of the bacillus itself or of its toxine. It also counteracts the toxine when mixed with it before injection into an animal. It is injected, therefore, into the human body, in cases of diphtheria, with the double object of rendering it immune to the further action of the poison and of counteracting the effects of the poison already absorbed. The most careful antiseptic precautions should always be taken, and the syringe sterilised by boiling before being used. The results obtained by this mode of treatment, both in this country and abroad, have been remarkably uniform, and of such a nature as to fully justify the belief that antitoxic serum is a remedy of far greater value in the treatment of diphtheria than any of its predecessors. Its effects on the course of the disease are very remarkable.[1] The general mortality is reduced by about one-third, and the mortality in tracheotomy by about one-half. Extension of membrane to the larynx very rarely occurs after the administration of antitoxine, and there is also a very sensible diminution in the number of laryngeal cases which require tracheotomy. Moreover, the remedy is of especial value in the very classes of cases which under any other treatment give the worst results, namely, in the very young, and in the laryngeal form of the disease. Thus the mortality of 488 laryngeal cases treated with

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[1] For fuller information on this subject, the reader is referred to the "Report of the Committee on the Antitoxine of Diphtheria," 1898, *Trans. Clin. Soc. London*, vol. xxxi.

antitoxine was only 28·8 per cent., whilst of 197 cases in which tracheotomy was performed nearly 60 per cent. recovered.

Two essential conditions to success are—(1) To commence the treatment at an early stage of the disease, and (2) to inject a sufficient dose of anti-toxine. It has been truly said that "a dose of 2000 units will usually secure a result on the first day which 50,000 will not effect on the fourth." The following figures, taken from the report of medical superintendents of the Metropolitan Asylums Board for 1896, quoted below, illustrate the importance of early treatment:—

No. of Cases.	Day of Disease on which Treatment was begun.	Mortality per Cent.
57	1st	5·2
406	2nd	15·0
557	3rd	21·9
579	4th	27·8
1165	5th and after	31·7

As regards dosage, no hard-and-fast rules can be laid down. Each case must be treated on its merits. There is every advantage in using the strongest serum obtainable. In mild or moderately severe cases coming under observation on the first or second day of the disease, a single dose of two or three thousand normal units may suffice; in severe cases larger doses should be employed. If definite signs of improvement do not follow within twelve hours, a second injection should be given. There need be no hesitation in doing this, as the remedy does not cause any material harm. Opinions are still divided as to whether it is better to push the remedy vigorously during the first forty-eight hours, or to give it in smaller doses over a longer period. The writer's personal experience is decidedly in favour of the former plan. In favourable cases there is a marked ameliora-tion both in the local and general symptoms. There is a rapid diminution of faucial swelling and distress. The pulse soon improves, and other constitutional symptoms subside. The spread of the false membrane is arrested, and it separates sooner than with any other mode of treatment. Nasal discharge, when present, is usually much diminished or disappears altogether. In laryngeal cases the necessity for tracheotomy is often avoided, and the results after tracheotomy are incomparably better than under any other circumstances. It is not at present possible to form a reliable estimate of the effect of antitoxine on the occurrence of paralysis, partly because under this mode of treatment a larger number of cases recover from the primary disease in which paralysis would be likely to supervene, partly on account of incomplete knowledge of the influence of dosage on the course of the disease.

The antitoxine treatment should be adopted in every case of diphtheria. As regards the prophylactic use of antitoxine, it should be borne in mind that the protection afforded is not of long duration. Its use should there-fore be limited to cases where the risk of infection has been great. In a certain proportion of cases, and with some specimens of serum more than others, the injection of antitoxine is followed by after-effects or complica-tions, which, although giving rise to some discomfort, are not serious. They are rashes, fever, and joint-pains, and usually occur from one to

three weeks after injection. The rashes frequently appear first at or near the site of injection, and may be urticarial, erythematous, or morbilliform. Desquamation often follows. They are often accompanied by fever and some general disturbance. Similar rashes may follow the injection of tetanus antitoxine and tuberculin. Joint-pains are much less frequent, but may be severe, and are generally accompanied by fever and considerable general disturbance. As regards the alleged injurious effects of antitoxine on the kidneys, causing anuria and nephritis, these complications are not more frequent in cases treated with antitoxine than in those which are not.

<div align="right">W. PASTEUR.</div>

ERYSIPELAS.

Syn., Fr., *Erysipèle;* Ger., *Erysipel; Rose.*

AN acute infective spreading inflammation of the skin, due to a streptococcus, and associated with general febrile symptoms. The subcutaneous areolar tissue may be simultaneously affected (cellulitis). Although typically an infection of the skin, the inflammation may also affect a mucous membrane, either primarily or by extension.

Etiology and pathology.—The disease is widely spread, but is more frequent in temperate and cold than in tropical countries. It usually occurs in the endemic form, but may assume an epidemic type. It is especially prevalent during the spring months and again in late autumn. Chief among the causes which favour its development are insanitary surroundings, more especially overcrowding, dirt, and defective drainage. Improved sanitation and the adoption of aseptic methods in surgical practice have led to a very material diminution in the number of cases, for whereas the disease was formerly the scourge of hospitals, it is now comparatively rarely to be found there.

The virus may be conveyed through the air, but it does not seem to act at any great distance. It adheres closely to clothes, bedding, furniture, etc., and may be conveyed by a third person. Women are said to be more liable to the disease than men. Age has no influence on its incidence. Among predisposing causes, the more important are chronic alcoholism, faulty hygienic conditions, debility after acute or chronic diseases, and diseases of the liver and kidneys. A constitutional predisposition may exist, and is sometimes hereditary, the patient usually suffering from repeated attacks of the disease. A wound, abrasion, or sore is the most important predisposing cause, and it is generally held that the disease is invariably caused by the infection of a wound. Recently delivered women are particularly susceptible to infection.

The determining cause of erysipelas is a streptococcus (*Streptococcus erysipelatis* of Fehleisen) which is held by most to be identical with the *Streptococcus pyogenes:* its peculiar manifestations in this disease being attributed to a certain degree of virulence. " It must be noted, however, that erysipelas passes from patient to patient as erysipelas, and purulent conditions due to streptococci do not appear liable to be followed by erysipelas. On the other hand, the connection between erysipelas and puerperal septicæmia is well established clinically. The conditions which produce the special degree of virulence in the streptococcus for the

occurrence of erysipelas are not yet fully known. In a case of erysipelas the streptococci are found in large numbers in the lymphatics of the cutis and underlying tissues, just beyond the swollen margin of the inflammatory area. As the inflammation advances they gradually die out, and after a time their extension at the periphery comes to an end. In the affected area there are the usual changes found in inflammation, great leucocytic emigration and serous exudation with formation of fibrin at places, but there is no suppurative liquefaction of the tissues" (Muir and Ritchie).

The streptococcus of erysipelas can be grown in pure culture outside the body, and may reproduce a true erysipelas when inoculated into human beings, as was done by Fehleisen in his endeavour to cure certain forms of malignant disease. The streptococcus stains with the ordinary aniline dyes and by Gram's method. The chains of cocci are short in the human body, but may attain a considerable length in artificial cultivations.

Morbid anatomy.—The post-mortem appearances in an uncomplicated case are by no means characteristic. The affected skin feels swollen, hard, and inelastic; the inflammatory redness disappears after death. Blebs, desquamation, and effusion into the subcutaneous cellular tissue are usually present. The internal organs are congested, and the spleen is sometimes much enlarged. There is usually cloudy swelling of the kidneys, which may also present evidence of antecedent chronic disease. In erysipelas of the scalp, subcutaneous abscesses are not uncommon. When death has been due to septicæmia or pyæmia, the visceral complications of these infections will be present. There may be septic inflammation of the pleura, pericardium, and occasionally of the endocardium. Meningitis, when present, is probably pyæmic, but it is also said to arise from an extension inward of erysipelas of the scalp. Infarcts may occur in the lungs, spleen, and kidneys, and there may be the evidence of a general pyæmic infection. Pneumonia is occasionally met with, whilst hypostatic congestion of the lungs is common.

Symptomatology.—The incubation period is usually between three and seven days. In Fehleisen's inoculations it varied between fifteen and sixty-one hours. Cutaneous erysipelas is described as traumatic or idiopathic, originating in the former case in connection with a wound, whilst in the latter no wound or abrasion can be discovered. The distinction between these two varieties is probably purely artificial; in any case their symptoms are the same. Idiopathic erysipelas is common about the face and scalp. The traumatic variety may develop wherever there is a wound, or the equivalent of a wound, of the skin or of a mucous membrane. The following description applies especially to erysipelas of the head and face. The invasion is usually quite sudden, and often marked by a rigor or vomiting. The temperature rises rapidly, sometimes to a great height, and the usual symptoms of fever, headache, thirst, anorexia, etc., are well marked. The chart of a typical case is shown in Fig. 35. The general symptoms are usually in direct proportion to the extent of the skin affection. This first appears simultaneously with or within a few hours of invasion as a sharply defined patch of redness, either in relation with a pre-existing wound or at the junction of a mucous membrane and the skin, especially the corner of the eye, the angle of the mouth, or the external auditory meatus. The affected skin is bright red, tense, painful and swollen, and pits on pressure. The inflammation extends in all directions. Its spreading margin is irregular, sharply defined, and slightly raised. Swelling of the subcutaneous cellular tissue is always marked, and

even in cases of moderate severity the face is much swollen, the eyes closed up, and the lines of expression obliterated, so that the patient is quite unrecognisable. Vesicles form over the inflamed area, and may run together to form blebs of considerable size. These ordinarily contain clear yellow serum, which may be blood-stained in virulent cases. After bursting, the bullæ dry up and leave adherent scabs. The cervical glands are always enlarged and tender, and there is usually some general swelling of the neck. Suppuration is uncommon. " Definite abscesses occurring in the skin or subcutaneous cellular tissue are most probably the result of a mixed infection, and this is not unlikely to be the case when they occur, as is not very uncommon, in the eyelids" (Watson Cheyne). The febrile symptoms usually continue unrelieved as long as the skin affection is spreading. After a few days the inflammation gradually subsides, and desquamation of the cuticle takes place. After erysipelas of the scalp there may be a temporary complete loss of the hair. Occasionally the
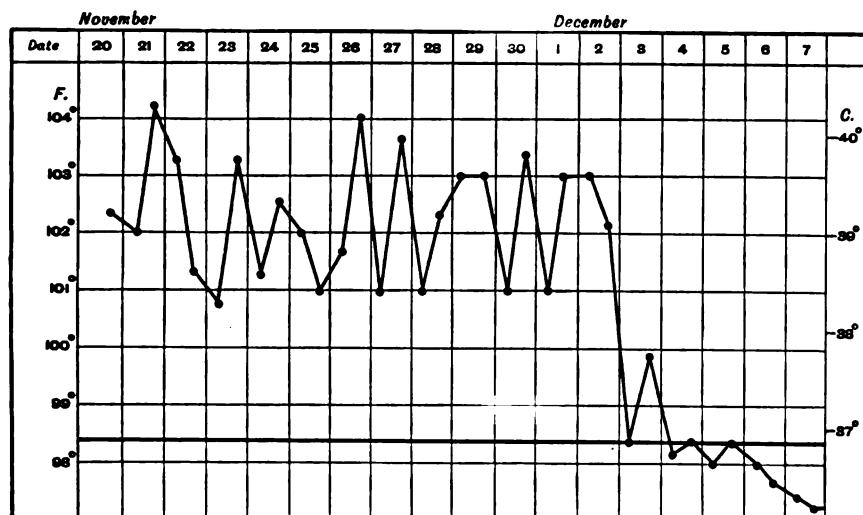
FIG. 35.—Temperature in erysipelas.

inflammation spreads from the head over the trunk and limbs in succession. In this more chronic form of the disease (*E. migrans vel ambulans*), which occurs more often in young children, the temperature is very irregular. Slight delirium at night is not uncommon, even in mild cases. In severe cases and in debilitated individuals, it is often a very prominent symptom. The constitutional disturbance varies much. It is usually slight in uncomplicated cases, but the gravest symptoms may supervene in old and debilitated persons, and in the subjects of chronic alcoholism. In some drunkards the delirium assumes a low muttering type, the tongue becomes dry, the pulse fails, and death is ushered in by deepening stupor and coma. In others there is intense headache with violent delirium, accompanied by extreme restlessness and delusions. Albuminuria is often present.

Erysipelas occasionally affects the mucous membrane of the mouth, fauces, and larynx, by extension from without; more rarely the disease originates in the mucous membrane. The fauces and pharynx in such cases are red, shiny, and œdematous, and there is marked glandular

swelling at the angles of the jaw. Bullæ containing turbid serum are often seen. They soon burst, leaving yellowish white membranous patches. Extension to the larynx is often very sudden, and gives rise to intense dyspnœa, which may be rapidly fatal, unless promptly relieved by suitable measures.

The duration of cutaneous erysipelas is variable. In uncomplicated cases the temperature often falls by crisis. This may occur as early as the fourth or fifth day, or be delayed for ten days or a fortnight. Simultaneously the inflammation ceases, and there is a general amelioration of symptoms. Convalescence is sometimes prolonged. When death occurs in simple erysipelas, it is usually due to exhaustion or to toxæmia.

Complications.—Some of these are purely local, or due to a direct extension from the original seat. One of the most important is local suppuration, which may lead to a general septic infection. Meningitis apart from pyæmia is rare, even in cases where brain symptoms have been prominent. Pneumonia and acute nephritis are occasionally met with. Delirium tremens may arise in drunkards. A condition of persistent œdema or elephantiasis sometimes follows repeated attacks of the disease. Eczema, lupus, and other chronic skin diseases are often much reduced, or even cured, by an attack of erysipelas, and a shrinking of sarcomatous and other tumours has also been observed.

Diagnosis.—In the fully developed disease this rarely presents any difficulty. But where the appearance of the rash is delayed, as sometimes happens, or where the disease originates in the hairy scalp, an early diagnosis may be attended by the greatest difficulty. In differentiating erysipelas from other cutaneous affections, reliance is to be placed chiefly on the mode of onset, the definiteness of general symptoms, and the characteristic appearance and behaviour of the rash.

Prognosis.—Simple cutaneous erysipelas is not a fatal disease, and healthy adults very rarely die of it. Advanced age, debility, renal disease, and habits of intemperance all influence the prognosis unfavourably. As regards the attack itself, the following are unfavourable signs :—Persistent high fever, early prostration, extreme restlessness, excessive diarrhœa, frequent vomiting, and violent delirium. Erysipelas spreading from the navel in the new-born is an extremely fatal disease.

Treatment.—The patient should be strictly isolated, especially in hospital practice, and suitable precautions taken by the medical practitioner and those in attendance on the patient against conveying the disease to others. As the disease tends to run a short and favourable course, it is certain that little more than good nursing is required in many of the cases. The general treatment should aim at maintaining the strength of the patient, and with this object a light and nutritious diet and a judicious use of stimulants are indicated. In severe cases, and in the old and debilitated, alcohol must be freely given. Restlessness, delirium, and insomnia must be met by sedatives, but where they constitute an alarming symptom, the best results will be obtained by the cautious use of morphine or hyoscine hypodermically. To bring down the temperature, cold or tepid sponging should be used in preference to antipyretic drugs, such as antipyrine and antifebrin.

It is very doubtful whether any drug administered internally has any influence on the course of the disease. The tincture of the perchloride of iron in doses of thirty to sixty drops every three or four hours has been highly recommended and very widely employed. The subjects of erysipelas

are remarkably tolerant of the drug. Local treatment should aim at excluding air from the inflamed area, relieving pain and tension, and if possible, at checking the spread of the inflammation. Many remedies, some of them of doubtful value, have been recommended for the latter purpose. Among these may be mentioned painting the skin with collodion, iodine, solutions of nitrate of silver, of perchloride or persulphate of iron, and more recently with ichthyol. Some of these, particularly iodine and ichthyol, often cause much pain. The injection of antiseptic solutions beneath the skin at several points just beyond the spreading margin is more rational, and seems deserving of further trial. Protection from the outer air is best obtained by painting the inflamed skin with flexile collodion, and after dusting it freely with fine zinc and starch powder, enveloping it in cotton-wool. Local pain is most effectually relieved by hot, moist applications. In many cases carbolic fomentations (1 in 40 strength) are very soothing. Boric fomentations and lead fomentations (liq. plumbi ʒij ad Oi.) are also valuable. Painting the skin with glycerin of belladonna in combination with fomentations has also given good results. All hot applications should be renewed frequently. Cold lead lotion and cold water applications may be used with benefit where the swelling is slight. Minute linear scarifications have been recommended where the tension is extreme, and gangrene is feared. Suppuration must be dealt with by appropriate surgical means.

<div style="text-align:right">W. PASTEUR.</div>

SEPTIC DISEASES.

Syn., Fr., *Maladies septiques;* Ger., *Wundinfections Krankheiten.*

SPEAKING generally, these affections are due to the entrance into the blood and tissues of certain living micro-organisms or of their products. In the large majority of cases the infection of the system starts from a previously existing wound or collection of pus in some part of the body. Their chief interest to the physician arises from the fact that they are essentially general diseases, and that they arise occasionally without any previous lesion, so far at least as can be ascertained by the most careful examination. The bacteria usually concerned in these affections are those commonly associated with suppuration, namely, the *Staphylococcus pyogenes aureus* or *albus* and the *Streptococcus pyogenes.* General infections have also been observed in association with the *Bacillus coli communis*, the pneumococcus, the gonococcus, and others.

Although the terms sapræmia, septicæmia, and pyæmia are of some value as indicating differences in the kind of infection, it must be borne in mind that, clinically, no hard-and-fast line can be drawn between them. Thus a streptococcic infection may present clinically — (*a*) Sapræmia, from the absorption of bacterial products, as for instance the case of a parametric abscess without general infection; (*b*) septicæmia, such as that which constitutes one variety of puerperal fever; and (*c*) pyæmia, in which metastatic abscesses develop in the course of a general septicæmia.

The paths of secondary infection are summarised as follows by Muir and Ritchie:—"First, by lymphatics. In this way the lymphatic glands may be infected, and also serous sacs in relation to the organs where the

primary lesion exists. Second, by natural channels, such as the ureters and the bile ducts, the spread being generally associated with an inflammatory condition of the lining epithelium. In this way the kidneys and liver respectively may be infected. Third, by the blood vessels: (*a*).by a few organisms gaining entrance to the blood from a local lesion and settling in a favourable nidus or a damaged tissue, the original path of infection being often obscure; (*b*) by a septic phlebitis with suppurative softening of the thrombus and resulting embolism; and we may add, (*c*) by a direct extension along a vein, producing a spreading thrombosis and suppuration within the vein. In this way suppuration may spread along the portal vein to the liver from a lesion in the alimentary canal, the condition being known as pyelo-phlebitis suppurativa."

SAPRÆMIA.

This is liable to occur wherever there is dead or injured tissue undergoing putrefactive changes in contact with a rapidly absorbing surface. It probably plays an important part in the so-called traumatic fever, and constitutes one of the varieties of puerperal fever. The severity of the symptoms varies with the dose of poison absorbed. The onset is sudden, with chill or rigor. The symptoms are in the main those of fever: thirst, headache, anorexia, rapid pulse, restlessness, and increasing prostration, leading to coma and death unless the source of the poison is removed by appropriate measures. Severe cases of pure sapræmia are decidedly rare.

SEPTICÆMIA.

In this form of septic infection the invasion of the body may proceed from a local site, as in puerperal septicæmia, or post-mortem or other wounds, or the disease may arise without discoverable local cause— idiopathic or cryptogenetic septicæmia.

Morbid anatomy.—The post-mortem appearances are those of rapid decomposition with visceral congestion. The blood is fluid and dark. There is marked post-mortem staining of the interior of the vessels. The heart is flabby. Ecchymoses in the serous membranes are common. The lungs are congested. The spleen is large and soft, and the liver and kidneys congested and swollen. Neither thrombi nor emboli are found. The signs of peritonitis are often present, particularly in puerperal cases. The changes at the site of inoculation or in the wound vary greatly.

Symptoms.—In a typical case, after wound infection the disease commences suddenly; within a few hours, or at most two or three days. The temperature either rises rapidly, with a severe rigor, which may be repeated, or the rise is more gradual, the rigor being replaced by chilliness. It usually remains high, with daily remissions, and sometimes with intermissions. The course of the temperature in a well-marked case is shown in Fig. 36. The pulse is rapid and feeble, and the heart soon loses strength. The tongue is red at the edges and dry on the dorsum. There is complete anorexia, and gastro-intestinal disturbances are common. There is usually more or less headache. Delirium may set in early and pass into coma, or the mind may remain clear to the end. Breathing is rapid, and there may be signs of general bronchitis, with a varying degree of lividity. The urine frequently contains albumin. Death may occur as early as the second or

third day. If life is prolonged beyond this, the patient passes into the typhoid state. The skin becomes sallow or jaundiced, and purpuric spots often appear. Intractable diarrhœa is apt to supervene, and death from exhaustion takes place usually within a week. The milder varieties of the disease usually occur in connection with suppuration and septic wounds. Septicæmia may complicate other acute diseases, such as diphtheria and typhoid fever, and occasionally supervenes in the later stages of Bright's disease and tuberculosis.

Diagnosis.—The diagnosis presents no difficulty where there is an obvious source of infection, such as a post-mortem prick or dissection wound. Where the source of infection is obscure the difficulty is often extreme. The discovery of streptococci in the blood may assist the diagnosis, but they are not necessarily present in the specimen obtained for examination, and septicæmia is not always due to streptococcus infection.

From sapræmia the disease can only be distinguished by the greater prostration which accompanies it. The symptoms of the two conditions

FIG. 36.—Temperature chart from a case of acute septicæmia ending in recovery.

are very similar, and moreover they are usually associated. The distinction from pyæmia rests chiefly on the acuter onset, more rapid course, more sustained temperature, and, later on, the absence of secondary abscesses.

Prognosis and treatment.—The prognosis in severe cases is extremely grave, especially in cases of acute puerperal septicæmia, which are almost invariably fatal. The general treatment should be directed towards maintaining the strength of the patient in every possible way. Among drugs, quinine is probably the most valuable. The hypodermic injection of anti-streptococcus serum has been largely used in cases of septicæmia with some measure of success. Its use should be limited to cases in which there is definite evidence of a streptococcic infection.

PYÆMIA.

Pyæmia may be described as that form of septicæmia in which the bacteria which invade the general circulation give rise to the formation of multiple abscesses in the internal organs, and in various other parts of

the body. The micro-organisms most commonly concerned are streptococci and staphylococci.

Etiology and pathology.—In the large majority of cases, pyæmia arises in connection with a pre-existing wound or injury, or in relation to some local disease process which lays the body open to invasion by one or other of the pyogenic bacteria. In this way, ulcers of the intestine, or of other mucous membranes, gonorrhœa, prostatic thrombosis, otitis media, empyema, the interior of the uterus after parturition or abortion, etc., may become the focus of infection. In very exceptional cases no primary focus can be discovered (idiopathic pyæmia). A very constant and, probably, an essential feature of pyæmia is the occurrence of septic phlebitis and thrombosis in a vein adjacent to the primary focus. The thrombus becomes impregnated with organisms, softens, disintegrates, and small fragments containing organisms are carried as emboli into the general circulation. These become arrested in the organs to which they are first carried, and there give rise to suppurative infarctions which may cause abscesses of considerable size.

The situation of the pyæmic infarctions and secondary abscesses is governed to some extent by the course of the blood stream. Wherever the infective emboli are discharged into the general venous circulation, the embolic abscesses occur chiefly in the lungs. They are often associated with septic pleurisy, probably by direct extension, and pericarditis and peritonitis may also occur. Sometimes infective particles pass through the lungs, and may cause foci of inflammation in the heart and kidneys. When the source of infection is situated within the area drained by the portal circulation, the chief secondary deposits are found in the liver (portal pyæmia). In cases arising as acute osteo-myelitis, the heart and kidneys may be the organs chiefly affected. Infection of the endocardium is very liable to occur, and may materially modify the character of the clinical features. Vegetations develop on the affected valve, and become covered with clot, portions of which may be carried to various parts of the body, where they give rise to suppurative infarctions, notably in the brain, spleen, and kidneys.

The general appearances of the body after death are the same as in septicæmia. The nature of the local lesions has already been sufficiently indicated.

Symptoms.—There may be general malaise with some fever for a few days before the onset of acute symptoms. In some cases phlebitis and venous thrombosis can be made out. In thrombosis of the lateral sinus there may be severe pain and tenderness along the course of the vessel, whilst in cases of wound infection local changes are generally present. Often the disease begins suddenly with a severe rigor, followed by profuse sweating and great exhaustion. During the rigor the temperature may rise to 104°, or higher, and falls again rapidly during the sweating stage. The fever continues with large remissions, interrupted at irregular intervals by fresh rigors. In the intervals between the rigors the pyrexia may be only slight, and it is not unusual for the temperature to drop below normal during the remission following a rigor. The constitutional symptoms are well marked. The expression is anxious, and the face soon grows sallow or jaundiced. Appetite is lost. Vomiting is common, and there may be troublesome diarrhœa. The tongue is dry. Prostration is marked, the breathing is hurried, and there is a rapid loss of flesh. Transient erythema in various parts of the body is common.

The pulse is frequent and weak. The first cardiac sound is usually feeble, and may become inaudible. Various cardiac murmurs may be heard ; these are sometimes functional, but may also indicate the presence of secondary endocarditis. The local symptoms vary considerably, and may be but slightly marked. When the lungs are affected there is cough and dyspnœa, and there may be signs of patchy consolidation with or without râles. Other cases present the signs of pleural effusion or of pericarditis. The spleen is enlarged, and may be the seat of acute pain as the result of infarction. There may be signs of general peritonitis, especially in puerperal cases. Abscesses in the kidneys usually give rise to pain and albuminuria, and sometimes to hæmaturia. Delirium is not uncommon whilst the fever is high, with a return of consciousness in the intervals. In some cases the mind remains clear for a considerable time. With the onset of the typhoid state muttering delirium is common. The duration of acute cases is often quite short, from six to ten days.

In the more chronic forms of the disease, visceral complications are less frequent, and suppuration is prone to occur in various joints, and in
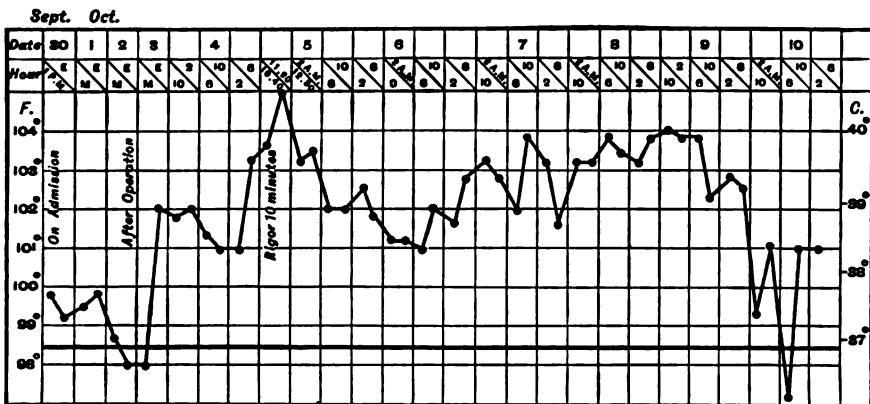
FIG. 37.—Temperature chart from a fatal case of pyæmia.

the muscles and subcutaneous tissues. The temperature is irregular, and chills and rigors may occur at long intervals. Some patients ultimately recover, whilst others eventually die of exhaustion.

The general symptoms of portal pyæmia do not differ from those described above. The type of the disease is always severe. The liver is always enlarged, and may rapidly attain to a great size. The spleen is also much enlarged. There is intense pain over the hepatic region, and marked jaundice and ascites are present in some cases.

Diagnosis.—This as a rule only presents difficulties in cases where the primary source of infection is obscure. In all suspected cases a careful search must be made. A localised osteomyelitis may easily be overlooked, as may also a gonorrhœa or a prostatic abscess. Where acute renal symptoms occur early, the distinction from acute Bright's disease is not easily made. Some cases present a somewhat close superficial resemblance to malaria, but the diagnosis should seldom present any real difficulty. Malaria rarely resists quinine. The resemblance of cases of more chronic type with marked diarrhœa to enteric fever is sometimes very close. Osler lays stress on the importance of marked leucocytosis in the differential diagnosis. Hæmorrhage from the bowel is rarely seen in

pyæmia. Cases of pyæmia have aiso been mistaken for acute tuberculosis. In arthritic cases the distinction from rheumatism rests chiefly on the persistence of the joint lesion, the absence of the characteristic sour odour of the perspiration, and the presence of other signs of pyæmia.

When meningitis or uræmia complicate pyæmia, the general symptoms may be to a great extent obscured by those of the local condition, and lead to errors in diagnosis. As regards ulcerative endocarditis, where endo-cardial murmurs are present, it may be very difficult to decide whether the vascular lesion is part of a general infection, or whether the general symptoms are not themselves due to a malignant endocarditis.

Prognosis and treatment.—The prognosis in the visceral forms is very grave. Cases of portal pyæmia hardly ever recover. The prognosis is somewhat more hopeful where only external abscesses occur. The general treatment is the same as in septicæmia. Both the primary lesion and secondary abscesses, wherever they are accessible, should be dealt with surgically, and if the infection is due to the streptococcus, the serum should be employed.

<div align="right">W. PASTEUR.</div>

ACUTE PNEUMONIA.

Syn., Croupous Pneumonia, Lobar Pneumonia, Pleuro-pneumonia, Pneumonic Fever.[1]

AN acute infective fever, apparently dependent on the invasion of certain micro-organisms, especially the *Diplococcus pneumoniæ* (Fränkel), or pneumococcus (of which there would seem to be several varieties), characterised by symptoms and signs referable to local inflammation of lung, and by grave constitutional, more particularly circulatory, disturbance.

History.—From early times pneumonia was spoken of as a separate disease, but the dividing line between true acute pneumonia and pleurisy was not so defined as it might have been. The predominance of lung symptoms and the post-mortem appearances naturally caused pneumonia to be regarded as a local lung process.

During the past half-century the infectiveness of pneumonia has come to be considered both at the bedside and in the laboratory. At the present day the infective nature of the disease is recognised by the large majority of competent observers. Discussion continues as to certain etiological relationships, but the main thesis as to its infectiveness is admitted,—the specific agent in its production being the *Diplococcus pneumoniæ* (Fränkel), or pneumococcus, and perhaps the *Bacillus pneumoniæ* (Friedländer). More than this, there is a growing consensus that the pulmonary aspect of the disease has loomed too much in the foreground. The disease is henceforth to be relegated to the group of acute infective fevers. The local (pulmonary) lesion is to be considered analogous to the throat lesion in diphtheria or scarlatina, or the intestinal lesion in typhoid. The local lesion is accom-panied, to a greater or less degree, in different cases, by constitutional infection. As we shall see later, the specific organisms have been dis-covered, not only in the lung but also in the pleura, pericardium,

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[1] The name Pneumonic Fever is preferred by the writer as the best descriptive term, both from the etiological and clinical standpoint. It is justified by the analogy of enteric fever.

endocardium, peritoneum, meninges, kidneys, spleen, and blood. Indeed, it has been demonstrated that the organisms may be recognised in these organs at a date prior to their appearance in the lung.

Etiology.—From what has just been said, it is apparent that the present-day conception of pneumonia has displaced some of the etiological views, or at least relegated them to a position of less importance. It will be convenient to consider the subject under two heads—(1) Specific (exciting) factors; (2) auxiliary (predisposing) factors.

1. **Specific factors.**—The claim of specific influence has been advanced on behalf of more than one organism. There is pretty general agreement that the most constant and certain is the *Diplococcus pneumoniæ* (Fränkel). The *Bacillus (Micrococcus) pneumoniæ* (Friedländer) is present in a considerable number of cases. These organisms may sometimes be discovered together, or the one may alone be present without any determinable difference in the clinical history. The two organisms resemble each other not a little, but are separable by staining and culture methods, and by inoculation experiment.

The *Diplococcus pneumoniæ* (Fränkel) is elliptical in form, or lance-shaped (*M. lanceolatus*). As found in the sputum, it is generally paired and encapsuled ("capsule-coccus"). A cover-glass preparation, treated in the usual way by glacial acetic acid, is readily stained by means of gentian-violet dissolved in aniline water (*i.e.* distilled water saturated with aniline oil. The diplococcus may be discovered sometimes in the saliva of apparently healthy persons, and for long in that of patients who have suffered from pneumonia. It has therefore been maintained that its causal influence is small. But its constancy in the expectoration of the pneumonic subject is opposed to this; and the local and constitutional effects produced by inoculation with a pure culture substantiate strongly the specific position. More recent observations (Eyre, Washborn) indicate that there are several different varieties of pneumococcus. The different varieties have been obtained from varying sources, *e.g.* the sputum of the pneumonic patient, the pus from the meninges in pneumonia, the lung tissue itself, pus from an empyema following pneumonia, and the saliva of the patient. These varieties have been shown to be possessed, not only of different biological characters, but of different degrees of virulence.

If their causal influence be admitted, how do the organisms obtain an entrance? This is effected by way of the respiratory passages. There is no reason to doubt the observation that the organisms are present on apparently healthy surfaces. In this view the organisms are frequently ranged in menacing line. It may be that the disease is caused by the presence of an unusually large army of these, or, as is more likely, by their successful invasion of tissues which have been weakened by one or other of the auxiliary causes, to be detailed presently. It is a fact of much interest that the organisms have been determined on the floor and roof in certain dwellings where pneumonia has been recurrent from time to time.

By way of the respiratory passages the lungs are reached, and here the more evident lesion is induced. But that this is not all is proved by the discovery of the organisms in pleura, pericardium, endocardium, peritoneum, meninges, kidney, spleen, and blood, and by the grave constitutional implication. The presumption is that the constitutional disturbance is the effect of a toxine produced by the organism. This so-called pneumotoxine has been separated in glycerine extract from cultures of the pneumococcus. When injected into animals, the toxine induces pyrexia and other grave

symptoms, and finally would appear to produce within the circulation another body possessed of antagonising properties, to which the name antipneumotoxine has been given. This antipneumotoxine, it is maintained, can be separated from the serum of pneumonic patients subsequently to the crisis. It would seem likely that the bone marrow is one of the seats of production of the immunising substance. Reference is made further to this aspect of the disease under the head of "Treatment."

It has been long recognised that pneumonia is endemic, or, at least, its occurrence is more frequent in certain localities. When a footing has been attained, it would appear never to leave a district entirely. This may depend on, among other causes, the fixity with which the organism clings to places once affected. As already stated, the pneumococcus has been discovered on the floor and roof of dwellings (prisons), and may be found, for more than a year, in the saliva of patients who have recovered. Natives of a district where it is common seem to suffer more than visitors. Its occurrence in *epidemic* form is well established. Many physicians have reported illustrations of this, as for instance the appearance of three or more cases in one household. Generally such instances have occurred in relation to overcrowding, as for example in prisons, workhouses, barracks, and schools. An epidemic of the kind occurred on board H.M. training ship *Caledonia* some seven years ago, when a large number of cases were admitted to the Edinburgh Royal Infirmary. Sometimes the outbreak has been associated with other epidemics, *e.g.*, the fatal pneumonia which was grafted on influenza during the recent epidemic of that disease, and similarly during the great epidemic in 1847. The question of degree of *contagiousness* is still a moot one. But there is reason to maintain that, within limits, the fact of contagiousness has been established. I have seen more than one instance in hospital where old inmates of the ward, suffering from other disease, have become infected by a pneumonic new-comer. Instances of the carriage of the disease to a third person have also been reported.

2. **Auxiliary factors.**—These are either (*a*) general, or (*b*) individual.

(*a*) *General.*—Climate seems to play *per se* an unimportant part. Pneumonia occurs frequently enough in all different climates. Its occurrence would seem to be influenced by variability rather than actual coldness of climate. Hence it is commoner in temperate than in very warm or cold regions. The seasonal variation in frequency is considerable, and differs in different parts of the world. In the United Kingdom, pneumonia is commoner during winter and spring than during summer and autumn, and, as a rule, during spring than during winter. This is probably a further expression of its dependence on sudden alterations of temperature, and the occurrence of chill.

Similarly, constant exposure to cold is less likely to predispose than sudden cooling after being heated, with perhaps accompanying fatigue. Country-people and sailors are less frequently affected than dwellers in busy centres, where overcrowding, insufficient ventilation, alcoholism, and privation are auxiliary agents of the first moment.

(*b*) *Individual.*—*Sex* is of interest, in so far as pneumonia is distinctly commoner in men than in women, while the fatality of the disease is greater in women. Regarding *age*, statistics vary somewhat. But summing those up, we may aver that it is especially common to 10 years of age, that it is less common thereafter till about 25, that it is common between this and 45, and, thereafter, is common enough till the close of life.

The previous health of the patient is an element of importance. It has

been calculated that not more than one-third of pneumonic patients can show a good record. The predisposing tendency of disease may be seen both as regards acute and chronic processes. Of acute, the most familiar examples are the fevers, in the wake of several of which pneumonia is apt to develop. Notably is this the case with influenza, typhus, and typhoid. Similarly, an injury to the lung, it may be a contusion or something more severe, is apt to be followed by pneumonia (contusion pneumonia). Or pneumonia may be dependent on the passage of foreign bodies into the lungs. Chronic disease, either of the respiratory apparatus or general, is a frequent precedent. Thus pneumonia may supervene on bronchitis or tuberculous disturbance of the lung, or albuminuria, or diabetes, or alcoholism, or nervous disease. The relationship of pneumonia to some of these is significant, and is further discussed under " Prognosis." Lastly, it is to be noted that a previous attack of pneumonia does not confer immunity. On the contrary, it seems to increase the liability. Cases are on record where many attacks (in one instance, as many as twenty-eight) have been passed through.

Morbid anatomy.— The morbid changes are centred especially in the lungs, but are to be sought for also in relation to a number of other organs.

The pulmonary process is essentially a fibrinous inflammation. It involves continuously one lobe or a portion of it, or may involve an entire lung or portions of both. An entire lung and as much as two-thirds of the pulmonary tissue of the other side may be implicated. Double pneumonia is, however, much less common than one-sided. Occasionally isolated patches may suffer, scattered irregularly throughout one or both lungs. On the whole, the right lung appears to be more frequently affected than the left. Certainly the lower lobes are affected more commonly than the upper. The inflammation results in the exudation of a solid material in the alveoli—the clinically-determinable consolidation.

Four stages in the inflammatory process may conveniently be recognised —(1) Engorgement or congestion; (2) red hepatisation; (3) grey hepatisation; (4) resolution or liquefaction.

Engorgement or congestion.—The lung is deep red in colour, changing to brighter red on exposure, and is unusually firm and heavy. It is moulded by the pressure of the finger, which squeezes out blood-stained fluid and less air than normally. As the process advances the air is more and more replaced by exudation. Microscopic examination shows a greater or less degree of desquamation of the epithelial cells lining the alveoli and engorgement of the capillaries. The duration of this stage may be reckoned at from twenty-four to thirty-six hours.

Red hepatisation.—The lung is of brownish red colour, bulky, firm, and heavy. The pleural surface is turbid, generally carries some fibrinous exudation, and may show small hæmorrhagic extravasations. The surface may be slightly marked by the ribs. There may be some fluid effusion in the pleural sac. In rare instances the pleural effusion is more abundant, and may be serous, seropurulent, or even purulent. On section, the lung is found to be solid—hepatised—in part or whole, as indicated above. In colour it is bright red, tending later to assume the appearance of red granite. Here and there hæmorrhagic areas may be discovered. Surrounding the hepatised areas there is often some evidence of œdema of lung tissue. From the cut surface there exudes a brownish red, muddy liquid. The bronchial glands are usually enlarged. Microscopic examination shows that the alveolar spaces are distended with a firm fibrinous

material, in which may be seen detached epithelial cells and red blood corpuscles in varying quantity, and one or all of the micro-organisms which have been described. The character of the exudation explains the clinical appearances of the sputum. The duration of this stage may be reckoned as some two to four days, the process passing gradually on towards the next stage.

Grey hepatisation.—The lung is now of paler hue, varying from greyish red to yellowish grey. The pleural surface generally shows more distinct fibrinous exudation. The organ is evidently heavy, weighing perhaps some two or three pounds more than normal. On section, the lung is solid as before. In colour it shows varying shades of grey, according as the exudation has become more or less decolorised, and is happily compared to grey granite. The surface has a granular aspect. The lung tissue tends to be more friable, and a cut portion sinks in water. The liquid which escapes is dirty grey in colour, and still more turbid. From the cut bronchioles, small casts may occasionally project. Microscopic examination shows that the exudation is less fibrinous, and therefore less tenacious. Leucocytes are present in abundance, in different degrees of fatty degeneration. The final resultant is the gradual replacement of the fibrinous exudate by a more fluid, flaky material.

Resolution or liquefaction.—The lung remains of greyish hue, and is conspicuously soft and friable. On section, the firm aspect has disappeared. The alveolar plugs drop out easily, and there wells in large abundance from the cut surface a more uniform, greyish yellow fluid—the débris resulting from the process of fatty degeneration. This material is readily absorbed, and little of it sees the light of day. Indeed, the whole course may be passed through without much expectoration. The exhibition of expectorants to aid in its removal has no pathological warrant, and is bad practice. The visible expectoration is largely bronchial in origin. In the course of a week from the commencement of resolution—in uncomplicated cases—the lung may have recovered its normal appearance without any trace of the grave disturbance through which it has passed.

Thus far we have considered the appearances in the course of a fairly simple pneumonia. Even here it must be admitted that the limits of the stages cannot be exactly fixed in every case. Further, in a given lung, at any one time, there may be evidence of two or even three stages simultaneously. Lastly, it is to be remembered that cases may abort, and correspondingly the anatomical changes stop short, say at the stage of engorgement.

From the pleural surface, the inflammation may pass to the pericardium, and, more rarely, to the peritoneum. The pericarditis shows the usual appearances of that condition, but the pneumococcus may be discovered in the fibrinous exudation. Endocarditis may also be present, either simple or ulcerative, and the specific micro-organism be discoverable. The right heart is generally distended with a firm clot, which may be traced far into the pulmonary artery. The branches of the pulmonary artery usually remain pervious throughout the whole course of the disease, and the circulation, if slowed, is maintained sufficiently. In the kidneys there may be evidence of nephritis. The pneumococcus has been discovered in the capillaries and veins. The spleen may be enlarged, and sometimes a croupous condition of the gastro-intestinal tract is found. Other foci of infective inflammation may be present as in the meninges. The anatomical appearances of these conditions are described elsewhere. All this points

to a systemic infection. It has, indeed, been suggested that the lung manifestations are not primary but secondary to the systemic infection.

Where the natural termination in liquefaction and absorption does not take place, there may be evidence of various morbid conditions. More especially, gangrene may occur, with characteristic odour and destruction of tissue, which are described elsewhere. Termination in suppuration, whether diffuse or localised (abscess), is not common. The pus may burrow in various directions, more particularly into the bronchi, through which it is evacuated. Or the pus may burst into the pleural sac, giving rise to one variety of empyema. Lastly, the process may sometimes remain chronic, the lung assuming a cirrhotic appearance. The relations of cirrhosis to the disease under consideration are not quite certain. It is difficult to say to what extent the lung was damaged before the attack of pneumonia. As has been suggested clinically, the pneumonic process may have been determined in a lung already disturbed. Doubtless this statement applies to those cases which have been supposed to become tuberculous in the wake of pneumonia. In some of these, at least, pneumonia was determined in a tuberculous lung, and the pneumonic condition first of all drew attention to the chronic consolidation. I have observed, in a number of patients who have died of pneumonia, tuberculous areas of varying sizes of comparatively old date. Had these patients lived, and the tuberculous condition been discovered later clinically, the condition might probably have been misinterpreted as a consequence of pneumonia. Caseation does not occur in such cases apart from tuberculous infection.

Symptomatology.—The clinical picture of acute pneumonia, or pneumonic fever, varies much. It varies at different seasons and in different localities. It varies with the age of the patient, and, especially, it varies according to the condition of the patient, precedent to the attack. There has been a tendency sometimes to speak of pneumonia as almost constant in its course and physical signs. Nothing could be a greater mistake. The more one studies cases of pneumonia, the more one recognises the wideness of variability. It will be convenient, first, to describe shortly the leading features of the disease as it occurs suddenly, in an apparently healthy adult under middle life, and then to indicate the more frequent deviations from this in different cases.

The *incubation* period has not been determined with certainty. Till recently, observation was not directed to the point. It is probably short, and has been approximately fixed at from one and a half to two days.

The *invasion* is sudden and heralded by a rigor of varying intensity, so that the patient can fix pretty well the beginning of the illness. The patient usually experiences severe pain in the side, often described as stabbing. This is referred commonly to the mammary or axillary areas, or to a corresponding point behind, or it may be lower down. It is increased by the respiratory movement, which becomes accordingly more shallow and frequent. The shallowness is protective, and the increased frequency is partly complementary to the shallowness, and partly the expression of the fever. The patient is manifestly dyspnœic, and speech tends from this cause to be gasping. Following the rigor, which may last ten to twenty minutes or more, a high pyrexia is registered.

The appearance of the patient at this stage, say on the second day, is characteristic. He generally lies on his back. The prostration is considerable. The face is flushed, it may be faintly cyanosed or dusky. The alæ nasi move actively and rapidly. The rate of respiration is evidently increased.

The expression is painful and anxious. Round about the mouth there is frequently an eruption of herpes labialis. The skin is felt to be intensely hot, the temperature reaching probably 103° to 104° F. The pulse is rapid, full, and bounding, though not quickened proportionately to the respiration rate so much as in other fevers. A short, painful cough shakes the patient, and is not easily restrained. Expectoration is scanty, consisting of a more or less blood-stained, air-containing mucus, of extreme viscosity, which renders discharge difficult.

The disease runs its course approximately in a week. During this time the temperature continues elevated, with morning remissions of perhaps a degree or so. Finally, it falls suddenly to the normal or below the normal in the course of a few hours, the crisis occurring, it used to be supposed, preferably on an odd day, the fifth, seventh, or ninth. While the pyrexia lasts, the patient's distress continues. More particularly there is gradual prejudice of the circulation, the pulse becoming soft, often dicrotic and irregular. Some degree of delirium frequently supervenes. The tongue is loaded with a white fur. Appetite and digestion are variously disturbed, the former being sometimes wonderfully maintained. The urine is high-coloured, sometimes contains albumin, and shows a marked diminution of chlorides. The physical signs, which develop in the lung with advancing consolidation, are also variable, and will be discussed more fully presently. With the critical fall of temperature the patient's distress quickly disappears, and the pulse improves correspondingly. Within a few hours he exchanges a state of grave malaise for one of comparative well-being. Convalescence is comparatively rapid and easy, the respiratory and circulatory disturbances disappearing from day to day.

The variability of the course makes it desirable that we discuss some of the symptoms in greater detail.

The invasion is not always so sudden as has been described. Pneumonia may supervene as a complication of some precedent condition, *e.g.* influenza or other fever, or it may develop in the wake of bronchitis, from which at first it may be discriminated with difficulty. Apart from this, premonitory symptoms of malaise, loss of appetite, sleeplessness, and the like, may occur during several days. Sometimes, in place of a pronounced rigor, there occurs repeated shivering or sense of chilliness. Occasionally the rigor is replaced by vomiting, sudden loss of consciousness, or convulsions.

General symptoms.—The *temperature* curve is not so constant as the foregoing description might suggest. In certain instances, notably in children sometimes, or where fever has existed before the development of the pneumonia, the ascent is less sudden. A day or two may elapse before the maximum is reached. Again, the temperature may run up to 106° to 107°. On the whole, however, hyperpyrexia is not common. The curve tends to be higher in children and alcoholic subjects. Although, as a rule, fairly constant, the pyrexia is subject to greater remissions apart from evident cause, resembling those in tuberculous pleurisy. Occasionally the pyrexia aborts as soon as the third day. Or there may be a sudden drop, what has been termed a pseudo-crisis, to be followed by a return of pyrexia. The true crisis may occur at any date, from the fifth day onwards, and no stress is to be laid on the supposed predilection for the odd days. It may be delayed till the end of the second week. While a *crisis* is to be looked for, the temperature may fall more slowly by *lysis*, the temperature swinging for days before finally settling to normal. The normal course of convalescence may be interrupted by the reappearance of pyrexia. This is

seldom a matter of importance. A true recrudescence is extremely rare. In very feeble subjects, pneumonia may be passed through without much pyrexia.

The *respiratory phenomena* may be more in the background. As we shall see presently, there are cases of pneumonia without evident lung symptoms. Pain in the side may not be complained of. As a rule, however, some degree of this is present, on inspiration. It is generally one of the first symptoms to disappear. The pain is most frequently referred to the areas which have been mentioned, but sometimes to the abdomen, or indeed to the other, that is the apparently healthy lung. The pain is doubtless pleural in seat, and to be attributed to an hyperæsthetic condition of the nerves in the inflamed area. As a rule, the rate of respiration is much increased, ranging from 30 to 60, or even more per minute. The relation of respiration to pulse is consequently disturbed. In place of the normal, 1 to 4·5, it may be as 1 to 2, or 1 to 1·5. The breathing is superficial and the expiration often grunting. Cough varies in intensity in different cases. It is a less conspicuous symptom in elderly patients. It is usually painful, and may induce serious circulatory perturbation, as may be observed on feeling the soft dicrotic pulse during the effort. The cough must therefore be regarded as a symptom of some moment. A troublesome spasm of coughing is sometimes thoughtlessly induced during the auscultation of a patient, by asking him to breathe deeply. It may likewise be induced during the effort of swallowing. The cough would seem to be abundant, in proportion as the pleural surface of the lung is implicated.

The *expectoration* is often most characteristic, but it may be absent, as in children. In typical form it is scanty, extremely viscid, so that the sputum jar may be turned over without loss, full of air bells, and of a colour ranging from saffron-green to dull red, or rust-like. The colour depends on the intimate admixture of blood in different proportion. Less altered red blood corpuscles may be determined microscopically, as also epithelial and mucous cells and fibrinous casts, usually minute, but sometimes of considerable size, showing evidence of dichotomous branching. The *Diplococcus pneumoniæ* may be demonstrated by the staining methods already described. Such characteristic expectoration may for a day or two be preceded by, or be intermingled with, sputum of muco-purulent character. Sometimes it is more evidently sanguineous, it may be even pure blood. At other times it is much more watery in character, as the result of accompanying œdema. The watery expectoration may assume a dirty, deep brown colour—the well-recognised " prune juice " expectoration, of evil omen. Chemical examination shows that the pneumonic sputum contains an excess of chlorides, and is wanting in alkaline phosphates, which are abundantly present in catarrhal discharge. Further, while in the latter there is more sodium than potassium present, in pneumonic expectoration sodium is present in considerable excess.

The *circulatory phenomena* are of the first importance. The outlook from day to day is affected more by the degree of prejudice of the circulation than by any other factor. The pulse rather than the lungs is the physician's weather-glass. Even in strong subjects the pulse rate is increased to 100 or more. In children this is exceeded greatly. In old enfeebled subjects it may not be so high. As a general rule in adults a marked increase of rate is to be viewed with suspicion, and carefully watched. Full and bounding at first, it tends to become softer from day

to day, and may be dicrotic. At this stage it is remarkable what a disturbing influence is exerted in weakly subjects by the effort of coughing —an instructive observation in respect of the necessity of the patient's avoiding all exertion. The gentlest movement of the patient from one side to the other may produce the same effect. Perturbation may be discoverable with the alternating movements of respiration. Increase of pulse rate, combined with advancing softness and irregularity in force and time—the beat, perhaps, not certainly countable at the wrist—is of grave omen. It may be the precursor of the crisis, but if this do not quickly supervene the hope of recovery is slender. Death may occur from circulatory failure at almost any point. It may be the final stage in the progressive stasis, which has just been sketched. The extremities become blue and cold, consciousness is abolished, and the patient dies from loss of hæmatosis. Or the heart may be suddenly overcome, and the patient die instantaneously, when there seemed little cause for alarm. This may be associated with exertion, or with the rapid extension of the pneumonic process. It is ultimately traceable to the action of the toxine.

The *blood* shows certain altered characters. The proportion of fibrin is estimated as increased from four to ten parts per 1000. The blood plates have been reported as much more abundant than normal. In most cases the leucocytes are increased, numbering perhaps twenty to forty thousand per c.mm. The increase occurs especially in relation to the large multi-nucleated neutrophiles, and, to a less extent, the large uninucleated corpuscles. The eosinophiles and the small uninucleated corpuscles, on the other hand, are diminished. The condition of leucocytosis appears early, and continues throughout the fever, passing away gradually after defervescence has occurred. It is believed that the non-appearance of leucocytosis is a bad indication. Difference of statement occurs as to the spleen. In some instances it may certainly be determined as enlarged, while more frequently there is no appreciable change. It seems a point of relatively slight importance, and in most cases minute investigation of this is inadvisable.

Nervous phenomena are often conspicuous. Thus, in children they may overshadow other symptoms. Ushered in by headache, vomiting, and convulsions, the condition may lead within a few hours to loss of conscious-ness. These features, curiously enough, may disappear as the lung symptoms become more evident. In adults, nervous disturbance is more frequently associated with apical localisation of the pneumonia. But in a considerable proportion of cases, independently of any such distribution, some degree of delirium occurs during the course of the disease, and is to be interpreted as the direct effect of the toxine. The delirium may be associated with marked elevation of temperature. Or there may be evidence of meningitic and other central complication, dependent on invasion of the meninges by the pneumococcus. Proof of this, about which it is by no means easy to be assured clinically, has been established by the discovery of the organism in the cerebral, and also, though less frequently, in the spinal meninges. In alcoholic subjects, the course of pneumonia is coloured by a preponderance of nervous disturbance of all kinds, more particularly by a noisy, violent delirium, requiring special care. Lastly, at or about the crisis, many patients suffer from a low muttering delirium, which may closely resemble the delirium of acute alcoholism, although there is no causal relationship of that nature. Doubtless the intense circulatory enfeeblement is in part responsible for this. When

head symptoms predominate in one or other form, the condition is some-
times described as *cerebral pneumonia*. Apart from, or accompanying,
these graver manifestations, tremors and irregular twitching of muscles
are common enough. The knee-jerk may be found to be lost.

The *digestion* is commonly much disturbed. As in other fevers, there
is apt to be anorexia. It is one of the most gratifying indications in the
course of pneumonia when the patient is able to take regular and sufficient
supplies of nourishment. The tongue is usually heavily coated with a grey
white fur, the edges perhaps remaining red. Sometimes it becomes dry
and hard, with cracking of the lips—the typhoidal tongue. This is not a
welcome appearance. Vomiting may usher in the attack, especially in
children and old subjects. Abdominal pain may be complained of, in some
cases due to intractable tympanites. The bowels tend to be constipated,
but, on the other hand, diarrhœa, even dysenteric in type, may supervene.
A trace of jaundice is commonly present, and may be observed as one of
the earliest of superficial changes. Those disturbances of the alimentary
tract may be conspicuous for days before there is evidence of lung disease.
Perhaps, like the graver nervous manifestations, they are to be attributed
to the direct influence of the pneumococcus on the digestive organs.

The *urine* is concentrated, of high colour, and yields a copious sediment
of urates. It is frequently albuminous, apart from evidence of complicating
nephritis. This is doubtless the effect of the organism on the kidney, as
albuminuria occurs with greater constancy in this than in most other
fevers. There is conspicuous diminution, or even arrest, of the discharge
of chloride of sodium during the pyrexic stage, with reappearance in excess
during resolution. The percentage excretion of urea is increased through-
out, and, conspicuously about the crisis, the amount discharged is absolutely
increased. Uric acid is similarly increased. If the patient happen to be
diabetic, there is a striking diminution in the secretion of glucose. This
must not, however, be interpreted in the patient's favour.

Approximately, 50 per cent. of pneumonic patients present herpes
labialis. It occurs usually quite early in the illness. Herpetic eruptions
elsewhere are much less frequent. It is rightly believed that a good
display of herpes is a favourable symptom. Flushing of the face is some-
times more marked on one side than the other. Some patients sweat
considerably from time to time during the pyrexic stage, without apparently
much relief from the pungency of the heat. The critical fall is generally
associated with marked sweating. Accompanying the diaphoresis, various
sweat eruptions may appear. More rarely, acne, urticaria, furuncles, and
ecchymoses have been recorded.

Inflammatory affections of joints, with effusion, occur occasionally, and
have been attributed to the invasion of the joint by the pneumococcus.
Similarly, painful affections of bones and periosteum are described.

Physical signs.—These are variable, both in character and date of appear-
ance. In some cases there are really no definite signs throughout the
whole course. In others, the signs develop in more marked fashion com-
paratively late in the course of pneumonia, perhaps even about the date of
crisis, and continue for a considerable time thereafter. This occurs in
adults sometimes, but often in children. In the larger proportion of cases
some of the signs to be detailed are determinable at one stage or another.
But the more experienced the observer, the less is he likely to insist on
having the complete picture in a given case.

Inspection may reveal, in addition to the unusual movement of the alæ

nasi and the hurried respiration, limitation of movement over one side. This may sometimes be visible while the night-dress is undisturbed. The limitation of movement becomes more evident on *palpation.* Sometimes a pleural rub is felt. The vocal fremitus may be recognised as increased.

Percussion in most cases yields some degree of dulness. Usually this can be elicited early. When the consolidation lies deeply, it may be obscured, or there may be a delay of some days before it is certainly recognisable. Quite as characteristic, and sometimes determinable before the dulness, is tympanites, some degree of which generally accompanies the dulness. Tympanites may be frequently determined in front, while the major dulness is behind, or the tympanitic area may be situated vertically higher in the lung. Often the physician has to rest his physical diagnosis —more particularly at the early stage—rather on the tympanitic than the dull percussion sound. As the consolidation advances, dulness becomes more evident, but still with a tympanitic ring in the surrounding parts. Still later, when the dulness clears away, the tympanitic element often conspicuously recurs.

The *auscultatory* phenomena vary greatly with the stage and extent and situation of the pneumonic consolidation. At the commencement, breath sounds may be enfeebled over a limited area, and this may be all. Or, on the contrary, breath sounds may be harsher than normal, gradually approximating the bronchial type. In the more regular cases, after the first day or two, a harsh, high-pitched variety of bronchial breathing— conveniently termed tubular — is the rule. The bronchial quality of breathing often continues for long after the critical fall of temperature. Quite early the inspiratory sound is accompanied by comparatively fine crepitations (*crepitatio indux*). In cases where there is an inflammatory condition of bronchial tubes, coarse accompaniments may mingle with or even obscure these. The crepitations, in most instances, are heard over a gradually widening area. In a day or two they may disappear, and the harsh tubular breathing be unaccompanied. Still later—often after the crisis—crepitation reappears (*crepitatio redux*), along with coarser, bubbling, even consonating accompaniments. The vocal resonance is usually increased at the time when the other indications of lung consolidation are present, and may have an ægophonic clang over the tympanitic area. With regard to all these physical signs, it is to be borne in mind that they necessarily diminish in intensity as one passes from the centre of more complete consolidation to the healthier portions of lung tissue.

The presence of complications may considerably modify the physical signs. When, for example, pleural effusion is present, the change in the physical condition of the parts will necessarily alter the signs, and the result may be a rather confused picture, in which the signs of one or other condition may predominate. The final recognition of the effusion is often made as the result of exploratory puncture, which is safe practice even in presence of pneumonia. Dry pleurisy is so essentially part of an acute pneumonia, that it requires no separate consideration.

The occurrence of abscess or gangrene, which is rare, will be suggested by certain symptoms and signs, which are discussed under the appropriate head. Examination of the heart sometimes shows enlargement of the right side. The heart sounds are heard with unusual loudness over the affected side of the thorax. Early in the attack there may be an audible accentuation of the second sound in the pulmonary area. Later, this may disappear. Sometimes murmurs develop in relation to the heart, more

especially far on in the illness, which pass away as the patient's condition improves.

Varieties.—Reference has been made incidentally to a number of these. Thus we have seen that pneumonia in children differs in many of its features from the adult type. Nervous phenomena (headache, convulsions, delirium, coma) are conspicuous. The temperature tends to run high, and the apex is more commonly affected. On the other hand, in senile pneumonia the temperature tends to be much lower, and circulatory embarrassment out of proportion to the apparent extent of lung mischief.

By *cerebral pneumonia,* as the name suggests, is meant that variety of pneumonia, whether occurring in adults or children, in which head symptoms predominate. The name *latent* or *larval pneumonia* has been applied to a group of cases in which slight or passing symptoms are present for a limited time, and where the diagnosis might be accepted with hesitancy were it not for the occurrence of other true cases, apparently in epidemic form, in the same neighbourhood, as for example in barracks or prisons. *Wandering* or *migratory* or *creeping pneumonia* describes a variety frequently enough seen—a considerable number of post-influenzal cases in the Edinburgh district were of this type—in which different areas of lung tissue, separate or continuous, become successively involved. The determination of such cases by physical signs is sometimes difficult. In *double pneumonia* we have the approximately concurrent involvement of portions of both lungs, with correspondingly greater disturbance of hæmatosis and circulatory strain.

Aside from such convenient enough terms, the attempt has been countenanced by some observers to separate a sthenic and an asthenic or adynamic variety. This is an unsatisfactory way of stating that the manifestations of the pneumonic fever, as of other fevers, differ according to the constitution and previous health of the person attacked. Similarly, we may safely drop from present-day nomenclature such varieties as rheumatic, malarial, typhoidal. The acute fever is one and the same in whomsoever it occurs, and such subdivisions tend to divert the mind of the observer from this fundamental conception. As in other acute fevers, patients sometimes fall into that low reactionless state which for convenience has been termed the typhoidal state, but that is no sufficient reason for speaking of a typhoidal variety. We have already seen that when pneumonia attacks a diabetic subject, it has certain peculiarities, and tends to lead to death—it may be with gangrene or abscess—but we are not, therefore, to describe a diabetic pneumonia as something distinct.

Complications and sequelæ.—It is to be premised, in the first place, that many phenomena which formerly, when pneumonia was regarded as a local inflammation of lung, were described as complications, are to be regarded as an expression of the invasion of the different organs by the morbific microbe. There is abundant post-mortem evidence for this way of stating the case. A number of these so-called complications have been, therefore, included in the preceding description of the clinical features. It is convenient, however, that reference should be made once more to some of these.

Taking the respiratory organs first, some degree of pleurisy forms a regular part of the disease (pleuro-pneumonia). But the pleurisy may be more considerable, and effusion occur either into the sac of the same or of the other side. In the fluid collection the pneumococcus has been discovered. Reference has already been made in dealing with the physical

signs to the difficulty of separating pleurisy with effusion from pneumonia. Empyema sometimes develops in the wake of pneumonia, still further confusing the diagnosis, which in such cases must rest ultimately on exploratory puncture. The empyema becomes evident in some cases only after the pneumonic phenomena have disappeared. There is reason for supposing that a precedent pneumonia is a commoner cause of empyema than was believed formerly. The clinical features of empyema are considered in their proper place. Diffuse suppuration may sometimes replace resolution, the patient tumbling into a typhoidal condition, from which he does not recover. Or abscess or gangrene of the lung may result. The symptoms and signs of these conditions are discussed in due course. Both are rare complications. The latter occurs more frequently in alcoholic subjects. Bronchitis may precede or attend the attack, and tends to aggravate the dyspnœa from which the patient suffers, and complicate the physical signs. Lastly, there is usually described a badly-resolving pneumonia, with persistent chronic infiltration. With regard to this there has been a good deal of discussion. It has been maintained that an acute pneumonia may fail to clear up, leaving a permanent residuum of consolidated lung, which may become tuberculous. It is to be remembered, however, that in many such cases no opportunity was available for the examination of the lungs of the patient before the acute attack. Were this possible, the probability is that in many instances a pre-existing infiltration would be determined, the pneumonic process attacking more readily the damaged lung. Again, there is much reason for believing that in some instances the process is throughout tuberculous, and that the appearances of the acuter stage have led erroneously to the diagnosis of an acute pneumonia.

Circulatory complications are not very common apart from the more general circulatory disturbance, which has been described already. Endocarditis is perhaps the most frequent. It may be either simple or ulcerative. Some 25 per cent. of the recorded cases of ulcerative endocarditis have been etiologically related to pneumonia. The diagnosis will necessarily rest on the development of a murmur during the course of the acute attack. Pericarditis occurs in a fair number of cases, especially in double pneumonia or extensive involvement of the left side, and more frequently in children than adults. It may be either dry pericarditis, or accompanied by serous or occasionally purulent effusion. The diagnosis is not always possible, but may be suggested by increasing faintness of heart sounds and further prejudice of the circulation. On the whole, it is a less serious complication than *a priori* might be anticipated. Thrombic conditions of veins and embolism of arteries occur occasionally.

It has been pointed out how largely nervous symptoms bulk in certain cases. In addition to these, true meningitis—dependent on the invasion of the meninges by the pneumococcus—occurs from time to time. It appears most generally during the pyrexic period, and may be accordingly missed, unless paralytic phenomena appear. Hemiplegia may supervene without traceable lesion, as described by several competent observers. Neuritis has also been reported.

Gastro-intestinal complications of different kinds occur. Some degree of icteric tinge is so common that it may almost be regarded as part of the pneumonic fever. Actual jaundice occurs in a smaller proportion of cases, being apparently commoner in right-sided pneumonia. It may develop at any period of the attack, but appears most commonly about the third or

fourth day. The explanation of the jaundice is not quite clear. A painful gastritis may be present, and occasionally a croupous colitis, with resultant diarrhœa. Parotitis, tending to pass on to suppuration, is one of the rarer complications. It has been observed sometimes in cases where ulcerative endocarditis has appeared. In most instances it is of evil omen.

Reference has been made already to the frequency of albuminuria. Actual nephritis is not a common complication. The arthritic condition which has already been described used to be regarded as a complication. Since the determination of the organism in the effusion, it is perhaps better regarded as one of the less common manifestations of the disease. It may supervene during the pyrexic stage or after the critical fall.

Diagnosis.—In the majority of instances diagnosis is not difficult. When, along with many of the symptoms of an acute fever, the physical condition of consolidation is discoverable, there is little room for doubt. But it must be borne in mind that a fair number of cases of pneumonia occur without traceable or at least characteristic physical signs, and that cases occur also in which the physical signs of pneumonia are present without anything else.

In concluding a diagnosis, attention will be directed especially to the following points:—The general appearance of the patient, his more or less flushed face, increased respiration out of proportion to pulse rate, activity of the alæ nasi, rapidly occurring and high degree of pyrexia (attaining its maximum it may be within thirty-six or forty-eight hours), the expectoration and the history of acute onset, with rigor or convulsion, and frequently pain in the side. The significance of these, more particularly the pyrexia, is necessarily less in the child than the adult. In the former, sudden and high degrees of pyrexia are determined by many less serious lesions. In addition to such manifestations, the absence of early symptoms, characteristic of other acute processes, as, for example, the sore throat or rash of scarlatina, has negative value of importance. In some instances the appearance of a herpes may bear corroborative import. If, along with such symptoms, one or two of the more obvious physical signs are present, the diagnosis should be complete. Of physical signs at an early stage, tympanites is to be looked on with no less suspicion than dulness. Limited areas of enfeebled breathing, with perhaps a faint crepitation on inspiration, or of conspicuously whiffing, bronchial breathing, or of increased vocal resonance, are of the utmost diagnostic value.

Real difficulty seldom exists with reference to pneumonia as occurring in a previously healthy adult. Mistakes are more likely from omission in patients already weakened by disease, as for example when pneumonia supervenes as a complication of one of the acute fevers, or of some other lung process, or of such chronic diseases as diabetes, kidney and heart disease, tuberculosis, or cancer, or after surgical operation. In any of these, an exacerbation of pyrexia, without other explainable cause, ought to lead the physician to a careful scrutiny of this possibility. Similarly, in the case of acute alcoholism or other delirious conditions without certain cause, it is good practice to make a point of excluding pneumonia. As has been pointed out already, there is a frequent relationship between delirium tremens and pneumonia.

In the case of children a double difficulty is encountered. On the one hand, from the preponderance of nervous, more particularly head symptoms and other constitutional distress, the advent of cerebral mischief, *e.g.* meningitis, or of one of the acute fevers, *e.g.* scarlatina, may be supposed.

On the other hand, the clear determination of physical signs is often harder in the child; the actual examination is more difficult, and the physical signs of different conditions are less clearly separable than in the adult. Thus it comes about that uncertainty may be experienced in distinguishing between croupous pneumonia and broncho-pneumonia or even pleurisy with effusion. The diagnosis will finally be made by a careful estimate of the preponderance of evidence along the lines already suggested.

In every case, it must be borne in mind that pneumonia may be present along with some other constitutional condition or preliminary lesion. Reference has already been made to the frequency with which pneumonia supervenes on certain constitutional affections. It is equally important to bear in mind that pneumonia may develop in connection with bronchitis, as in a considerable number of instances, or in relation to tuberculosis, as has been already described.

It may be convenient to rehearse that of diseases other than pulmonary, with which pneumonia is likely to be confused, the most important are meningitis, typhoid, typhus, general tuberculosis, septicæmia (especially in old subjects), and perhaps scarlatina (in the young). Of pulmonary diseases with which it might be confused, the most noteworthy are capillary bronchitis, broncho-pneumonia, acute tuberculosis, pleurisy, empyema (especially in the child). It is not the regular cases of pneumonia which are likely to cause difficulty, but cases aberrant from the classic type, either at the commencement—as the pneumonia of old subjects, which starts insidiously; or of children, presenting exaggerated nervous disturbance; or aberrant throughout their course, as when the typhoidal state supervenes; or aberrant as regards distribution, *e.g.* wandering pneumonia; or as regards physical signs. The diagnosis of complicating affections has, for the present, been sufficiently considered, and is further dealt with under the several appropriate headings.

Prognosis.—The prognosis is generally grave. The mortality of pneumonia varies much in different statistics, but at the best it is sufficiently high to make the prognosis an anxious one. Taking for our basis of calculation the collective statistics of various observers in many countries, we may fix 14 to 20 per cent. as the death-rate. The mortality fluctuates much in different places and at different times.

The character and course of the disease varies much with the seasons, and the prognosis in a given case may be fairly influenced by the character of precedent cases, about the same time and in the same neighbourhood.

The immediate prognosis is determined in all cases by a consideration of the pulse and heart from day to day and hour to hour, rather than by the temperature or the lung condition. The heart suffers directly from the pyrexia, as in other fevers; and the consolidation of so large an area of lung tissue puts an extra strain on the heart in a variety of ways. Further, there is reason to assume that the toxines act with especial prejudice on the circulatory organs. Advancing softness of the pulse is ground for most careful watching. Marked dicrotism justifies considerable anxiety. A pulse, palpably influenced by slight natural movements, such as that of inspiration, or by coughing, is a grave indication. A feeble and irregular pulse, hardly countable at the wrist, is of bad omen.

The prognosis is influenced much by the condition and constitution of the patient. Thus it is more grave in patients after middle life. In previously healthy adults it is much more favourable. In otherwise healthy children, it is still more so. In constitutionally feeble

subjects, more particularly at the two extremes of life, the prognosis is bad.

The disease is less common in the female sex, but when it occurs the outlook is less favourable. Female mortality is distinctly higher. The prognosis in pregnancy is very grave, though death does not certainly follow. Abortion is apt to be induced, sometimes with alarming hæmorrhage.

Certain precedent illnesses are conspicuously prejudicial, for example, influenza. During the recent epidemic of influenza this was frequently remarked. Patients too often succumbed, not to the influenza, but to the complicating pneumonia. Alcoholic individuals make bad subjects for pneumonia, and the prognosis is correspondingly graver. The presence of chronic disease of heart, or kidney, or other organ adds much to the gravity. In the case of diabetics who are attacked by pneumonia, the prognosis is most unfavourable. The amount of glucose excreted falls quickly, and it may be thought the patient is doing well. But comparatively suddenly he may die of circulatory failure.

The local distribution of the affection is not unimportant. Thus a double pneumonia, *cæteris paribus*, warrants a more serious prognosis. Even here the issue is far from being certainly fatal. Apical pneumonia seems more fatal than basal. A good appetite and continued power of assimilation are most satisfactory indications. An abundant eruption of herpes facialis may be looked on with favour. Absence of leucocytosis has been interpreted unfavourably. A rapid increase of the small uninucleated corpuscles, and the reappearance of the eosinophiles occurring about the crisis, would seem to point to a satisfactory termination.

The occurrence of complications renders the danger more imminent. Thus the supervention of œdema, as evidenced by the appearance of a watery, so-called prune-juice expectoration, already described, is of bad import. The appearance of fœtor of breath and fœtid expectoration, pointing to gangrene, is most unfavourable. The prognosis of abscess of the lung is discussed more fully under a separate head.

Treatment.—The treatment of pneumonia should be guided by the principles which are applicable in the conduct of other kinds of acute fever. The more fully this conception is before the physician, in approaching a given case, the better for the patient. The pneumonic fever is a short, acute fever, with a liability to certain accidents, more especially circulatory failure. Its treatment is that of an acute fever, with a jealous guard over the heart. The finger on the pulse is the better instrument than the stethoscope over the lungs. Treatment divides itself naturally into two sections:—

1. **Prophylactic.**—This aspect of the treatment of pneumonia is warranted by the occurrence of the disease in epidemic form. So many instances of this have been reported in workhouses, prisons, and other institutions, on board training-ships, and even in private dwellings, that the duty of disinfection must be apparent. The well-known example of the Bavarian prison at Amberg is especially trenchant. During the first five months of 1880, out of 1150 prisoners, no less than 161 were attacked by pneumonia, and of these forty-six died. Another severe epidemic occurred in the same prison within ten years. Further, there was isolated from the floor of the prison, an organism apparently identical with the pneumococcus— though this is not quite clear—and the disease was reproduced by inoculation. The same organism has been discovered in other badly-ventilated dwellings. All this points to the necessity for the rigid enforcement of

hygienic measures in the building and ventilation of such establishments, and the adoption of measures for disinfection where one or more cases have occurred. There is similar need for the enforcement of rules for disinfection of the expectoration. There is sufficient reason for the belief that in the past we have been too lax in such measures.

2. Therapeutic.—It may fairly be asked whether, with all our knowledge of the actual cause of the disease, we are further forward in this aspect of treatment. Awkwardly enough, the mortality from pneumonia has not fallen coincidently with the advance of our knowledge. Still this must not be held to deprive of significance the recent therapeutic endeavours based on the etiological fact. If the organism is the actual cause of the disease, and prophylactic measures have failed to prevent its entrance, the organism must be opposed within the body. This may be attempted theoretically in one of two ways. Either we may seek to destroy the organism directly, or we may antagonise those products of its growth and development which are toxic to the patient.

The endeavour has been made to realise the first purpose by intratracheal injections, *e.g.* of naphthol, by intrapulmonary injections (directly into the consolidated area), *e.g.* of perchloride of mercury, and by inhalations of certain volatile agents, *e.g.* iodide of ethyl. Up to the present the results have not been so completely satisfactory as to justify the recommendation of one or other method. Still they have not been so discouraging as to forbid the possibility of future success along such lines.

The second conception, namely, that of antagonising the products of the organism, has been elaborated by a number of observers. We have already seen that the pneumococcus probably affects the system through the production of a poisonous albumin. The so-called pneumotoxine presumably induces pyrexia and other grave constitutional disturbance, until, it would appear, there is produced within the circulation another body possessed of antagonising properties, so-called antipneumotoxine. It is maintained that immunity can be conferred on an animal—for some six months—by the introduction into a vein, or subcutaneously, of the glycerin extract from a culture, or of the filtered culture itself. It would seem that the serum of such immunised animals can in turn confer immunity on other animals, and, what is of still greater practical moment, can arrest the disease, if injected sufficiently early after infection. It has been shown also that the serum of patients suffering from pneumonia—removed shortly after the crisis—possesses this immunising and curative property in respect of inoculated animals. Encouraging results have also been reported in the human subject. Thus de Renzie has used serum, prepared according to Pane's instructions, since 1896, in grave cases of pneumonia, and reports that his former mortality of 24 per cent. fell under the treatment to 9 per cent. After injection of a sufficient quantity of serum, a remarkable fall of temperature occurred. Often enough there was a return to the normal temperature, which was maintained, although the lung process continued determinable. The improvement in the general condition of the patient was noteworthy, although the clinical progress of the local lesion was not apparently modified.

It is to be observed that Pane's serum appears to have protective powers against certain strains or varieties of pneumococcus and not against others.

While the serum method can hardly be reckoned sufficiently mature to warrant its general adoption, there is reason to anticipate a satisfactory development on this line in the near future.

Short of the consummation of such rational methods, we have to fall back on general principles of wider application. In commencing the treat‑ment of pneumonia, the physician will do well to think of it less as a lung disease than as an acute continued fever of comparatively short duration. It is of the first importance that the patient have an abundant supply of fresh air. A draught is less to be feared than the close, overheated rooms in which pneumonia is often treated. The morbid dread of fresh cold is a fatal mistake for the patient. The first point is, therefore, that there be an abundant and direct supply of fresh air, with as much sunshine as possible. This is essential in all fevers, but especially so in a fever accompanied by a local pulmonary lesion, which robs the patient of a large area of oxygenating surface. It is remarkable sometimes how quickly a feeble, depressed circulation improves by the correction of faulty treatment in this respect. And such results are always attainable without the access of the much feared draught.

The next indication is to husband the patient's strength with vigilance, and, in particular, to guard against circulatory failure. The dietary should be that of fever. Remarkable differences occur in respect of appetite and power of assimilation. One patient declines everything within the first day or two, another takes milk and soups almost with avidity. In the latter case there will be little difficulty, and ordinary meal hours may be adhered to. In the former, measured quantities of simple, nutritious fluid food must be given at regular intervals, say every three hours, with no less care than drugs are exhibited. Sometimes a grain or two of calomel, or a corresponding amount of grey powder, makes a wonderful improvement in a flagging appetite.

In most cases, after the first two or three days, alcoholic stimulants will be found helpful. Of these, diluted brandy or whisky is the most service‑able. They are given advantageously along with milk—often, best of all, with boiled milk—or as egg-flip, or with tea or coffee. Sometimes champagne picks up the patient more rapidly and efficiently. The quantity of alcohol will vary much. In less urgent cases a tablespoonful or two every six hours may suffice. When the condition is more serious, the same quantity may be required every two hours, or more frequently. Some patients do perfectly well—possibly even better—without alcohol throughout. The chief guide to the exhibition and the dose of alcohol is the pulse. It is when the full, bounding pulse of the first day or two is replaced by the soft and approximately dicrotic beat, that stimulants are indicated. As the dicrotic character becomes more evident, and the feeble, perhaps irregular, wave comes to be disturbed by each movement of the patient—notably by each cough—there is imperative call for a proportion‑ate increase in the frequency and quantity of alcoholic stimulant. Elderly and obese patients, those in debilitated condition, and especially alcoholic subjects, require such assistance earlier, and in larger doses, than those who have been previously vigorous. There is considerable danger in withholding stimulants from the alcoholic class.

Next in significance to alcohol come cardiac tonics. The same guid‑ing rules are applicable here. During the first two or three days, and in simpler cases possibly throughout, these may be unnecessary. But with advancing prejudice of the circulation, as evidenced by the changes in the character of the pulse already referred to, their value is great. The most generally helpful is strophanthus. This is exhibited conveniently in say 10-minim doses of the tincture, three to six times daily. Digitalis may be

used similarly, although the former seems, as a rule, preferable. In some instances, strophanthus may be helpful combined with strychnine. In the presence of more urgent circulatory failure, the more frequent administration of strophanthus is indicated, and the effect may be hastened by its subcutaneous use (strophanthin $\frac{1}{100}$ gr.) In such emergency, greater reliance is to be placed on more diffusible stimulants, such as ether, camphor, caffeine, by subcutaneous injection. With a patient *in extremis* from threatened circulatory failure and grave dyspnœa, this treatment may be supplemented by the exhibition of oxygen.

The relief of the chest pain is urgently called for in most cases. Its removal improves the patient's general condition marvellously, and indirectly relieves the respiratory and circulatory distress. To this end, warm poultices, turpentine stupes, or, for some patients, an ice-bag or the cold-water coil—the choice will depend largely on the patient—are serviceable. In some instances, particularly in powerful and plethoric subjects, local leeching or cupping, dry or wet, according to circumstances, is more useful. Or the desired effect may be best attained by the subcutaneous injection of morphine, in the absence of evident contra-indication. The objection sometimes urged against its administration, on the score of interference with expectoration, lacks pathological support. On the contrary, the use of morphine is further suggested in relation to the harassing, effectless cough, which unnecessarily disturbs the patient's rest and often seriously perturbs the circulation. Sanction for its exhibition is afforded by the cardiac condition. The drug will be used with moderation, and discontinued as the necessity diminishes.

Restlessness and sleeplessness are symptoms which require the utmost consideration. Much may here be gained by attention to lightness of bed-clothing, coolness of the sick-room, and the free entrance of fresh air. I have seen oxygen cylinders ordered for the relief of a patient, while the atmosphere of his room was stifling in the extreme—an irrational proceeding surely! Remarkable relief from restlessness may be achieved by the careful use of the wet-pack, which may be complete or partial according to circumstances. The one point to be attended to is, that the patient be excluded from effort of any kind during the procedure. If this be managed, most salutary results may be anticipated. So beneficial in respect of restlessness has this method proved, that some physicians are strong in the recommendation of tepid baths, from which it is reported that even better results are obtained. Personal experience does not warrant my recommendation of the method, in the carrying out of which there must always—at least in private practice—be some difficulty in preventing all effort on the part of the patient. In addition to these simple measures, morphine, in the moderate dosage which has been sanctioned on other grounds, may exert a salutary influence. Chloral, say 15 or 20 grs., may prove of the greatest service, by affording a few hours' calm sleep, which removes the restlessness and steadies the circulation as nothing else can. The chloral may be advantageously combined, sometimes with a claret-glassful of toddy. Sulphonal or trional may be similarly used, especial care being had to the thorough solution of the former in hot diluted spirit. Such a dose given opportunely would sometimes seem to be the determinant of the critical fall of temperature—the patient waking from a restful sleep with, perhaps, almost normal temperature.

Of antipyretics, in the limited sense, there is seldom need. Hyper-

pyrexia is not a clamant symptom, and there is no call to interfere with the ordinary pyrexial cycle. The simple method of wet-packing already referred to may well be considered in relation to this. Cold baths are seldom indicated. If the occasion demand the use of drugs, quinine or antipyrine will be found the most trustworthy. The method formerly much in vogue of commencing the treatment of pneumonia with aconite or other cardiac depressant, will rarely be found expedient, and, like the classic thorough-going blood-letting, is in most cases contra-indicated, the full, bounding pulse of the early period being only too rapidly replaced by the compressible vessel. In some cases, considerable relief to the patient, without counterbalancing disadvantage, is obtained by the free exhibition of the liquor ammonii acetatis from the first.

Consideration will be paid to unusual symptoms as they supervene, and their treatment undertaken in the light of the indications already premised, due regard being had to the age and condition of the patient. More particularly, the occurrence of complications and sequelæ, such as bronchitis, empyema, pulmonary abscess, gangrene, nephritis, delirium tremens, must be recognised and met as speedily as possible. The actual treatment necessary in different cases must vary, and is considered in detail under the appropriate head.

During convalescence certain tonics prove helpful, according to the condition of the patient, such as quinine, iron, strychnine, arsenic, cod-liver oil. Alcohol plays a useful part in this direction, whether it has been necessary earlier or not. About the critical fall, and for some time thereafter, wine or light beer will prove of service. The length of time the patient is to be kept in bed depends upon the constitution of the patient, the state of the circulation, and the local condition. There is much irregularity in the rate of improvement in different cases, conspicuously so as regards pulmonary signs. Here, too, the pulse is a better gauge than the local signs. When convalescence is sufficiently established, there is nothing to be gained by prolonged confinement of the patient. On the contrary, convalescence is often remarkably hastened by a change to the country. The choice of such change will depend on the residence, constitution, tastes, and purse of the patient. Having regard to the liability to recurrence, the physician must see that the cure is made as thorough as possible, and all rational lines of prophylaxis followed in future.

<div align="right">R. W. PHILIP.</div>

TETANUS.

Syn., Fr., *Tetanos ;* Ger., *Starrkrampf.*

TETANUS is a specific infective disease, due to the presence and multiplication of the bacillus of tetanus, characterised by an affection of the central nervous system, which gives rise to persistent tonic spasms, with brief violent exacerbations.

History.—Carle and Rattone were the first to show that tetanus was transmissible from man to animals, and hence of an infective nature. Nicolaier in 1885 was able to cultivate the organism in impure form outside the animal body, and with these cultures was able to set up in rabbits, guinea-pigs, and mice a disease apparently identical with tetanus in man. He was also able to show that small particles of soil obtained from the streets or from cultivated land, when inoculated on white mice,

were frequently capable of setting up a train of symptoms which strikingly resembled what one observed in experimental tetanus. He ascribed the disease to the presence of small slender bacilli, with round spores at one of their extremities. It was not till 1889 that Kitasato succeeded in separating this organism in a pure form, and proved definitely the relation of this bacillus to the disease. He found that it was an anærobic bacillus, which would not grow in the presence of oxygen, and which flourished best in a hydrogen atmosphere at the temperature of the blood (37° C.). This organism is readily stained by most of the ordinary dyes, and Gram's method is very useful for demonstrating its presence. The bacillus in its vegetative state is actively motile, and may form long threads which undergo segmentation and become motionless when the process of sporulation commences. At one end of each of the rods a highly refractile point is observed, which becomes larger and larger until it causes distension of the bacillus, in which it is developed, and thus is formed what is known as the "drum-stick" bacillus. These spores require a temperature of 100° C., 15 hours in 5 per cent. carbolic, or 3 hours in 1 per cent. corrosive sublimate solution, for their destruction.

It has been found that the tetanus bacillus is localised entirely to the region of inoculation, and never invades the blood or other organs of the body. This striking phenomenon can be explained only by the circumstance that the bacillus at first multiplies at the point of inoculation, and there generates an extremely virulent poison, which is absorbed, and then affects the nervous system. Kitasato has been able to separate this poison from cultures of the bacillus, and by its means to set up the train of symptoms characteristic of the disease. Sidney Martin has shown that the bacillus produces in cultures a ferment toxine, an albumose, and an acid body, all of which probably play a part in the production of the symptoms. He has also been able to separate these toxines from the organs of tetanus cases, which supplies a most important corroboration of the relation of this bacillus to the disease.

Behring and Kitasato in 1890 succeeded in rendering animals immune to this disease, and found that their serum contained an antitoxine capable of completely neutralising the tetanus toxine, and which was in all other respects analogous to the diphtheria antitoxine.

Etiology.—The origin of the disease is due to the entrance of the tetanus bacillus and the production at the seat of inoculation of a specific toxine, which affects specially the motor centres of the nervous system. Careful examination has failed to discover the presence of the organism in the blood or internal organs, and everything goes to show that the process, as in the case of diphtheria, is a purely local one, while the systemic effects are due to the absorption of the poison. The organism usually finds its entrance through an obvious wound, but this may be of the most trivial description, such as the bite of an insect, a mere scratch, or the puncture caused by subcutaneous injection. The organism, as one would expect, has a better chance of finding an entrance in cases of severe or lacerated wounds, burns, or where foreign bodies are lodged in the tissues. The occurrence of the disease is most frequently to be feared when the parts have been exposed to contact with earth and dirt, but this, of course, presupposes the presence of the specific organism in these. The bacillus, as has already been mentioned, is found most frequently in cultivated soil, and it has been stated occurs specially in the manure from horses and in the sweepings from stables. In this relation some experiments by Roux

and Vaillard may be noticed, which would seem to indicate that the tetanus organism itself is unable to set up the disease. They found that the spores of the tetanus bacillus, when they had been freed by washing from the toxine, were unable to affect even very susceptible animals. The addition of a small quantity of the toxine, or the addition of the products of other microbes, or even the bruising of the tissues locally, sufficed, however, to allow the inoculation to set up a fatal attack of tetanus. These experiments show the importance of the local element in the disease, and the important part which the pus organisms, which are so frequently present, play in the process. It is indeed probably owing to the absence of suppuration that we must ascribe the less frequent occurrence of tetanus which followed the use of antiseptics, since, as we have already stated, the ordinary antiseptics are not sufficiently powerful to destroy the tetanus bacillus spores.

The disease has been divided into two forms—the traumatic, where the process can be traced to a wound, and the idiopathic or rheumatic form, which was supposed to be due to exposure to cold. Since, however, we have come to recognise the infective nature of the disease, the number of cases occurring, classified under the latter heading, has tended to become less and less. The disease is more common in men than in women, and occurs more frequently in warm than in temperate regions.

Morbid anatomy and pathology.—There is usually present hyperæmia of the cerebral nervous system, often with small hæmorrhages, which occur specially in the motor centres. It has been stated that the bronchi are frequently the seat of catarrhal changes, and it has been suggested that this may be the point of entrance of the tetanus organism in idiopathic tetanus (Babés).

Symptomatology.—The disease is characterised by the occurrence of tonic spasms of the voluntary muscles, commencing in those of the face and neck, and gradually extending to all the muscles of the body. The most characteristic symptom of the disease occurs when the muscles of mastication are affected—the temporal and masseter muscles being contracted, and standing out in bold relief, so that the jaws are tightly clenched, giving rise to the popular name of the disease—"lockjaw." The scientific designation of this condition is trismus, and it is most important in the diagnosis of the disease. When the muscles of expression are affected, a peculiar and most typical appearance is presented, which is described as the risus sardonicus. Paroxysms of clonic spasms supervene on the tonic spasms at a later period of the disease, and are usually set up by some external irritation acting through any of the senses. There is frequently observed towards the end of the case, fever and rise of respiration and pulse rate. Sleeplessness usually prevails during the course of the disease.

Diagnosis.—The disease is recognised by the nature of the spasms and the history of the case. A bacteriological examination of the pus may be made either microscopically for the characteristic organism, or by the inoculation of a mouse at the root of the tail, which in cases of tetanus usually dies in the course of two or three days, exhibiting the characteristic symptoms of the disease.

Prognosis.—In the milder form of tetanus, which has been termed chronic, a considerable proportion of the cases recover, but in the more acute cases the prognosis is very unfavourable.

The severity of the disease appears to vary inversely with the period of

incubation, the longer the interval which has elapsed between the origin of the disease and the onset of the symptoms, the milder the form of attack. Those cases whose incubation period is twelve or fourteen days, in which the temperature does not rise over 39° C. with little dyspnœa, are mild in their character, and may usually be successfully treated by serum therapy. The acute cases with an incubation period of from five to seven days, with a temperature over 40° C., with rapid appearance of the spasms, are much less hopeful cases for treatment.

Treatment.—The treatment up to quite recently has been simply that of meeting the symptoms, and attempting to keep the patient alive during the course of the attack. Nourishment must be given regularly, and to procure rest and overcome the sleeplessness, chloral hydrate has been given in large doses. The subcutaneous injections locally of 1 per cent. carbolic acid were at one time strongly recommended. This treatment was based upon the local action of the antiseptic, and upon the fact observed by Kitasato that this substance destroyed the tetanus toxine. More recently the antitoxine discovered by Behring and Kitasato has been used in this disease, but it must be acknowledged, as pointed out by Kanthack, that the successful cases which have been recorded appear to be those more chronic forms of the affection, a considerable proportion of which recovered under former methods of treatment. The want of success with this antitoxine, as compared with that observed in the treatment of diphtheria, is undoubtedly due to the remedy being administered at a much later stage of the disease. At the period when trismus appears, when the disease is usually recognised, the disease is not in its initial stages, but has already advanced, the toxines having already combined with the nerve cells, probably of the motor centres. The administration of the antitoxine acts by uniting with the toxine, and thus prevents its combining with the nerve cells, but when injected at this late stage it can practically only prevent the action of any further toxine which may be absorbed. If we could only diagnose the disease at an earlier stage, experiments on animals show that the results obtained would be as satisfactory as those obtained in the case of diphtheria.

A modification of the antitoxine treatment has more recently been introduced by Roux and Borrel. They found that by intracerebral injection of the antitoxine, a much larger proportion of guinea-pigs, which had received a lethal dose of toxine, could be saved than if the serum had been introduced subcutaneously. Thus they were able to save thirty-five out of forty-five guinea-pigs when they received the injection into the brain, while out of seventeen which received the antitoxine subcutaneously only two recovered. This mode of treatment is still upon its trial, but the laboratory experiments would certainly lead us to expect that a certain number of the subacute cases which would otherwise die may possibly be saved by this method.

The use of the tetanus antitoxine for prophylactic purposes has been found very efficacious for horses in certain parts of France, where these animals frequently succumb to this disease after undergoing the operation of castration. This suggests the advisability of administering prophylactic injections of the antitoxine where one case out of a number exposed to the same conditions has developed symptoms of tetanus.

G. CARTWRIGHT WOOD.

EPIDEMIC CEREBRO-SPINAL MENINGITIS.

THIS is an acute febrile disease occurring epidemically, characterised by marked nervous symptoms due to inflammation of the membranes of the cerebro-spinal system.

History.—Epidemics of this disease were first recognised at the beginning of this century, and since that period they have been observed from time to time in different parts of Europe and in the United States. In 1846 it appeared in many workhouses in Ireland, but England and Scotland have remained remarkably free from the disease. Early in 1886, Netter and Fränkel published almost simultaneously descriptions of an organism associated with this disease. They found in primary cases of meningitis an encapsulated coccus, occurring either as diplococci or as chains, which could be cultivated on agar-agar at the temperature of the blood, and which presented all the characters of the pneumococcus of Fränkel. In addition, this organism was able to set up in white mice and rabbits a fatal disease precisely similar to that observed on the injection of the pneumococcus. The introduction of this organism into the brain of certain animals gave rise to an inflammation similar to that observed in this disease in the human species. It must be admitted, however, that the material obtained from different cases varied greatly in its virulence. This form of meningitis occurs not only as a primary affection, but has also been found on a number of occasions as secondary to pneumonia. The pneumococcus has now been separated from quite a number of undoubted cases of the epidemic forms of the disease by a series of reliable observers, but the etiological relation of this organism is still unsettled, as another very characteristic organism has also been observed in some of these cases. Weichselbaum found the pneumococcus in two out of eight cases, but in the six others he observed small hemispheres with flattened opposed ends greatly resembling gonococci, not only in their appearance, but also in the fact that they were usually found within the body of the cells. To this organism he gave the name of *Diplococcus intracellularis meningitidis;* this organism is also found, according to Netter, frequently in association with the diplococcus in these cases, but it sometimes occurs alone.

Etiology.—It is most generally believed not to be directly contagious, although it almost invariably occurs in the form of an epidemic. The discovery of a microbe apparently associated with this disease has, however, led many to support its contagious nature. Netter explains the fact that, as a rule, those in contact with a case are not affected with the disease, by pointing out that the infective material is usually shut up in the cranial cavity, and that only those cases where the organism occurs in the nasal discharge and in the pus from the ears and eyes are probably infective. The advocates of the contagious point of view direct attention to the fact that those attending on the sick have in a number of cases contracted the disease, and also that not unfrequently a number of cases occur in the same house; in addition, they assert that the origin of an epidemic may sometimes be traced to an imported case of the disease.

Children are most frequently affected, although others up to the age of sixty may contract the disease. The disease is more widely prevalent in temperate zones, and is said to occur more frequently in cold than in hot weather.

Morbid anatomy and pathology.—The characteristic feature of the disease is an inflammation of the membranes of the brain and spinal cord, especially of the arachnoid, which is usually covered with a yellowish deposit of lymph over this membrane at the base of the brain and the anterior part of the medulla oblongata. The ventricles and arachnoid spaces are filled with serous effusion, while the sinuses are filled with dark-coloured blood. The membranes of the spinal cord are also affected in a similar manner. Congestion and œdema of the lungs is sometimes present along with congestion of the spleen and liver. Rigor mortis is said to be of long duration.

Symptomatology.—One of the most characteristic features of the disease is the abruptness of the seizure and the rapidity with which the symptoms develop. The patient suffers from extreme nervous shock, cephalalgia and intense pain referred to the back of the head and neck, which ultimately invades the extremities, accompanied by spasmodic contraction of the muscles. The pain does not appear to be increased so much by direct pressure, every effort of the patient being directed to avert movement and preserve a state of immobility. This is indicated by the peculiar and characteristic attitude which is usually observed in this disease. The head is thrown backwards on the nucha, so as to lie almost at a right angle to the spine, which is extended and sometimes even arched as in tetanus, a condition which it somewhat resembles owing to the rigidity of the muscles which tend to maintain the patient in this position.

Eruptions appear on the skin at an early stage of the disease, on the second or fourth day, which vary greatly in their character in different epidemics. These may consist of raised lenticular rose-coloured spots, or extensive purpuric patches, usually on the trunk or extremities, while a regular herpetic eruption frequently occurs on the face.

If the patient recovers from the condition of collapse, a state of reaction usually sets in, when the temperature may rise from 100° F. to 103° F., and frequently a general amelioration of the symptoms is observed, which raises hopes which are, however, but seldom realised. Delirium is rarely absent during the course of the disease, and frequently the patient lies in a state of coma.

As a result of this disease we may have hemiplegia or paraplegia, due probably in the one case to a cortical lesion, and in the other case to a spinal lesion. Deafness or sometimes a low form of inflammation of the eyes may occur.

Diagnosis and Prognosis.—The history of the case and the symptoms usually leave no doubt as to the nature of the disease. It is quite probable that in the later stages the serum of the patient might be used for purposes of diagnosis. The mortality in this disease is very high, probably on an average 60 per cent. succumbing, but apparently the death-rate varies considerably in different epidemics. The prognosis must always be unfavourable.

Treatment.—In view of the infective nature of this disease, isolation and disinfection ought to be carried out. To relieve the headache and diminish excitement, the patient should be kept in a cool, dark, well-ventilated room; the head should be shaved and ice applied to it, and also to the neck and back if necessary. Opiates may sometimes be used in the early stage of the disease, but probably do not affect its course.

G. CARTWRIGHT WOOD.

BUBONIC PLAGUE.

AN epidemic communicable disease caused by the presence of a specific bacterium—*Bacillus pestis*—in the blood and tissues, and characterised by fever of an adynamic type, polyadenitis, buboes, and a very high mortality.

History and geographical distribution.—Introduced from the East some centuries before the Christian era, plague was at one time well known in Europe, where, during the Middle Ages, the constantly recurring epidemics caused an enormous mortality. With the advance of civilisation, and consequent improved hygiene, it gradually died out. With one exception (Portugal), it has not been seen in Europe since 1841, when it visited Constantinople for the last time. A small epidemic occurred in the Russian province of Astrakan in 1878 and 1879, but speedily died out. It finally disappeared from England in 1679. The Great Plague of London (1664–65) destroyed 70,000 of the 460,000 inhabitants of the city of that day. Until 1899 it had never been seen in America, nor in the southern hemisphere. Until a recent date, it was confined, so far as known, to Arabia, Mesopotamia, Persia, India, China, and Uganda.

Etiology.—The conditions under which plague becomes endemic are fairly well known; they are closely akin to those favouring epidemic outbursts of typhus exanthematicus, that is to say, personal and domestic filth and overcrowding. Plague never becomes epidemic in the presence of municipal and domestic cleanliness.

Predisposition.—*Sex and occupation* may have some influence as affecting liability to infection, but they have no very special bearing on susceptibility. Possibly old age has a certain protective influence. Previous attacks insure immunity for a short time only; they seem, however, to progressively diminish the gravity of subsequent infections.

Soil and altitude have no influence on the character or diffusion of the disease.

Temperature.—High atmospheric temperatures, especially if accompanied by drought, and very low atmospheric temperatures, tend, for the time being, to suppress epidemics.

Bacteriology.—The cause of the disease has been proved to be a minute bacillus, closely resembling in morphological characters the bacillus of chicken cholera and those of certain other septicæmias. It was discovered by Kitasato and Yersin in the Hong Kong epidemic of 1894. It occurs principally in the characteristic buboes, in the different viscera, and, more scantily, in the blood. It is also present in the alimentary canal, urine, and sputum. The bacillus is easily demonstrated by smearing the pulp of one of the buboes on a slide, fixing with alcohol or heat, and staining with an aniline dye. The ends of the bacillus are rounded off, and take the stain more deeply and readily than the intermediate portion, giving the bacterium a dumb-bell appearance. It can be cultivated on blood serum, on agar, and in bouillon. It does not liquefy gelatin. The disease can readily be conveyed to many of the lower animals by inoculation, either from the glands and discharges of a patient, or from cultures. Rats and mice are particularly susceptible, but guinea-pigs, rabbits, dogs (?), and many other animals readily take the disease both by inoculation and contagion, and also by the introduction into the stomach of cultures or of food containing the germ.

Infectivity.—Plague is not a very infectious disease; there is little

risk, therefore, to medical attendants and nurses in a clean, well-ventilated and roomy hospital. In dark, overcrowded, dirty native houses, however, when the disease has once been introduced, it rapidly spreads. The exact conditions in which ordinary circumstances determine diffusion are not known with precision; but it would seem probable that the infection is communicable to walls, floors, furniture, and clothing, and that it can be acquired from these, as well as more directly from close proximity to patients actually suffering with the disease. A remarkable and significant circumstance in connection with plague epidemics in man is, that before the disease appears among the people the rats are attacked; they come out of their holes and die in hundreds—in fact, for the time being, they become exterminated in the district. The affected rats contain the *B. pestis* in abundance, and their carcases exhibit the characteristic polyadenitis and other pathological features of plague. It is probable, therefore, that the rat is an important agent in diffusing the disease.

Epidemic diffusion.—In following the lines of human intercourse the disease somewhat resembles that of cholera; but, as compared to that disease, on the whole, the diffusion of plague is much slower, its incidence even more capricious, and, when established, its hold distinctly more tenacious. It tends to hang about a district or town for two or three years, picking out from time to time particular houses—"plague houses" —or areas which it decimates, and subsequently passing on to others previously and, apparently, capriciously spared.

Morbid anatomy.—Post-mortem rises of temperature, and muscular contractions like those occurring after death from cholera, are sometimes observed. The brain and meninges are congested; occasionally blood is found extravasated into the substance of the organ. Ecchymoses occur in all serous membranes. The lungs may present evidences of bronchitis, of hypostatic pneumonia, more rarely of croupous pneumonia; occasionally hæmorrhagic infarcts and even abscesses are found. The right heart and veins are distended with feebly coagulated or with fluid blood. The liver and spleen are enlarged. The intestinal mucosa is congested, presenting here and there punctate hæmorrhages and, occasionally, particularly towards the lower end of the ileum, hæmorrhagic erosions. The kidneys and perinephritic tissues are congested. The mucous membrane of the ureters and bladder may be dotted with small ecchymoses. The lymphatic system is invariably affected, the glands and, occasionally, the lymphatic trunks, being inflamed and swollen. The inflammatory effusion around the buboes is often abundant; it is sero-sanguinolent in character. The lymphatic glands contain the bacillus, sometimes mixed with the bacteria of suppuration, in great profusion. If death have occurred early in the disease, the signs of adenitis may not be so pronounced.

Symptoms.—After an incubation period of from two to eight days, with or without a prodromal stage characterised by malaise, feverishness, and perhaps pains in the groins, the disease sets in with extreme lassitude, severe headache, drowsiness, vertigo, perhaps vomiting and fever. Severe rigor is not a usual symptom. The face acquires a peculiar expression; it becomes haggard; the eyes are sunken and staring, the countenance sometimes expressing fear, sometimes indifference or bewilderment, sometimes hilarity. The patient, if walking be attempted, staggers as if drunk, moving about in a dazed condition. Temperature rapidly rising to 103° or 104°, or even higher. the face becomes bloated, the eyes red and ferrety the hear-

ing dulled; the swollen and furred tongue quickly dries, sordes accumulate about the mouth, thirst becomes intense, prostration complete. Delirium, or typhoid stupor, and the various nervous phenomena of the typhoid state, rapidly ensue. Vomiting, diarrhœa, or constipation may any of them be present. The spleen and liver are swollen. The urine is scanty. Albuminuria, though sometimes, is not always a prominent feature; like many of the clinical symptoms, this is different in different epidemics. The pulse, at first full and bounding, rapidly becomes small, dicrotic, and fluttering. At this stage the patient may rapidly sink and die from asthenia or from sudden syncope. Should the patient survive, in about two-thirds of the cases, some time between the second and fifth day—in a small proportion of cases it may be as late as the eighth or ninth day—buboes develop; they appear usually on the groins (70 per cent.), less often in the axilla (20 per cent.), still more rarely, but especially in children, at the angle of the jaw (10 per cent.). Occasionally they are present from the outset. These buboes are generally single; both sides, however, may be affected, and very often there is evidence, in the tenderness elicited by pressure, that the more superficial bubo is associated with a similar adenitis of the deeper abdominal glands. The buboes vary in size from a hazel-nut to a goose's egg, or even much larger, and are often very painful. The surrounding connective tissue and superjacent skin participate in the inflammation, and become red, swollen, and infiltrated. Boils, carbuncles, and purpuric extravasations are occasional features, being more common in some epidemics than in others. In favourable cases, on the appearance of the bubo, profuse perspiration sets in, and is accompanied by a rapid defervescence of fever and clearing away of the other symptoms. The bubo, however, continues to enlarge and finally softens and bursts, discharging pus and evil-smelling sloughs. On the other hand, suppuration may be delayed for weeks; or it may not occur at all, the bubo slowly resolving. Convalescence, when it does set in, commences usually between the sixth and tenth days, although subsequently there may be much secondary trouble from sloughing of buboes, from boils, or from pyæmic conditions.

Abortion invariably occurs in pregnant females, the fœtus presenting evidences of the disease. A peculiar type of pneumonia, hæmoptysis, and other forms of hæmorrhage, are sometimes a feature of specially malignant epidemics. Death in plague usually takes place from the third to the fifth day; but in that form which has acquired the name "pestis siderans," it may occur within the first twenty-four hours—in twelve hours even.

Pestis ambulans.—During epidemic plague, as with other diseases of the same class, milder cases, in which the patient is able to be about, occasionally occur.

Pestis minor.—Epidemics of a disease associated with fever and buboes, in every respect resembling true plague except in the absence of a high mortality, have been recorded from time to time as having occurred independently of, or as having preceded or followed, true plague. Their exact etiological relationship to malignant plague has not been definitely settled; there is a feeling among epidemiologists that in some way the virus of these mild cases may become intensified, and that in this way pestis minor may culminate in the more serious disease

Mortality.—The mortality in plague varies from 50 to 95 per cent. It is usually greatest at the beginning and height of an epidemic. Judging from recent experience in Hong Kong, it is less in Europeans than in

Asiatics; doubtless this is owing to the superior stamina of the former, and to the better attention and treatment which they receive.

Prophylaxis.—Municipal, domestic, and personal cleanliness is the best preventive of plague. Theoretically, quarantine ought to be efficient against its introduction; but, depending as quarantine does on the good faith of so many, and, in the case of this disease, on the exclusion of affected animals as well as affected men, in practice it must prove very fallible indeed.

On plague appearing in a community, hospital accommodation on a suitable scale should be at once provided, and daily house inspection, both for the ensuring of cleanliness and for the discovery of the sick, instituted and conscientiously carried out. The sick as soon as discovered should be removed to hospital, and the house from which they came disinfected, cleansed, and for a time shut up. Any house of little value, and provided it be otherwise practicable, should be destroyed by fire.

All rats should be killed by trap or poison, and their bodies burned. This measure, which, judging from the well-established fact of the extreme liability of these rodents to plague, and from their habits, is a measure of the first importance, has hitherto been systematically ignored in attempts at plague eradication. My impression is that a plague epidemic will continue in a place so long as any rats survive, and that when all rats are dead it will cease to spread and die out spontaneously. Manifestly, so simple a measure as the extermination of the rats is one of the first things to be attempted on the appearance of plague in a community, or better, in anticipation of the advent of the disease.

Plague fomites—including clothing and dejecta—should be disinfected by heat or destroyed by fire.

No one should be allowed to enter a plague house or hospital unless on important business. The attendants on plague patients should be careful to avoid hanging over their patients unnecessarily; they should take their food in a separate room; they should use disinfectants frequently and freely; and they should be specially careful never to handle patients or their fomites if they have wounds or scratches on their hands unprotected by an efficient dressing. With these precautions, attendants on plague cases are not likely to catch the disease.

Treatment.—Careful nursing, feeding, and stimulation are requisite in every case of plague. If there be constipation at the outset, one full dose of calomel is said to be serviceable in checking vomiting. For restlessness, delirium, and sleeplessness, hypodermic injections of morphine, early in the disease, are invaluable (Lowson); they must be given, however, with circumspection. Severe pain in the buboes is also best relieved by small hypodermics of morphine. Alcohol, strychnine, ether, or ammonia are of use and necessary when the heart is flagging. Diarrhoea, if urgent, is best treated by frequent 10-gr. doses of salol. High fever must not be treated by antipyrine and similar depressing antipyretics; they are dangerous in the extreme. Sponging of the body, and ice or cold applications to the head, are the safest as well as the most effective antipyretics. Buboes may be treated at first with applications of glycerin and belladonna; later, when fluctuating, they should be incised and dressed with iodoform. Iced beer, iced stout, and particularly ice-cream, are much appreciated by patients; they were of the greatest service in the Hong Kong epidemic.

Recently Yersin has brought out a serum which he maintains is an effective immunising as well as therapeutical agent in plague. It is

prepared by the repeated injection of cultures of *B. pestis* into the horse. In time the serum of the inoculated horse acquires antitoxic virtues *quâ* the bacillus. Of twenty-six cases treated with his serum in China, Yersin claims to have cured twenty-four. The rabbit, he says, can be rendered immune by this agent; moreover, if an unprotected rabbit be inoculated with a virulent culture of the bacillus, and subsequently, within a reasonable time, be injected with a sufficient dose of the serum, the progress of the disease is arrested, and the animal, otherwise sure to die, recovers. Later experience of Yersin's serum in Bombay does not bear out the favourable reports from China. Haffkine has also introduced a prophylactic serum vaccine, prepared from dead cultures of the bacillus; it has been extensively used in India, and is favourably reported on.

<div align="right">PATRICK MANSON</div>

CHOLERA.

A SPECIFIC, communicable epidemic disease, characterised by serous vomiting and purging, cramps, algidity, suppression of urine, a high mortality, and the presence of a special bacterium in the alvine discharges. It is endemic in certain parts of India, and possibly elsewhere. Following the lines of human intercourse, it extends from time to time as an epidemic to many parts of the world.

History and geographical distribution.—Although there is evidence of the existence of this disease in India from remote antiquity, its special nature was not recognised by European physicians until the sixteenth century. The great epidemic extension of 1813, during which cholera spread over nearly the whole of Asia, first drew marked attention to the subject. It was not, however, until 1830, when cholera visited Europe for the first time, that it became an object of careful study. Since that epidemic, 1830–32, there have been at least five other great European epidemics—1848–51, 1851–55, 1865–74, 1884–86, and 1892–95. Great Britain was involved in 1832, in 1848, in 1854–55, and in 1866, but not since. The last two European epidemics, although during them a considerable number of cases were imported, did not take root in this country. In 1832, and since, cholera has many times extended to America and to parts of Africa.

A study of the genesis of these various epidemics shows that cholera enters Europe by one of three routes—(1) by the Caspian and Russia; (2) by the Persian Gulf through Syria, Asia Minor, and Turkey; (3) by the Red Sea, Egypt, and the Mediterranean ports.

Etiology.—The home of cholera is said to be in Lower Bengal, where it is present at all times and at all seasons. Thence, from time to time, it spreads as an epidemic over India, occasionally extending by the routes just mentioned to Europe, Africa, and America.

In its extensions it follows the lines of human intercourse, travelling no faster than man travels. It never originates spontaneously in absolutely isolated spots, and rarely in places comparatively though not entirely isolated from the rest of the world. Thus it is unknown in Australia, New Zealand, the islands of the South Pacific, the Cape of Good Hope, the West Coast of Africa, the Orkney and Shetland Islands, the Faroe Islands, etc. From these circumstances it is justifiable to infer that

cholera is not the result of some meteorological influence, or in any sense an air-borne disease, as was at one time supposed; but that it depends on a specific germ which clings to man and is transported solely by him, either in his body, or in his clothes, or in some of his other belongings. At the same time experience has shown that it does not pass directly from man to man. Unlike smallpox, measles, and similar diseases, cholera is not contracted through simple proximity to a patient. Evidence of the most convincing character has shown that it is generally, if not always, a water-borne disease; that its germs, contained in the discharges of the sick, are first introduced into water, and then, in this medium, gain access to the intestinal canal of man. This being the case, we can understand how, when cholera is first introduced into a community, those insanitary conditions which favour fæcal contamination of the water supply also favour the spread of the disease. Knowing this, we have an explanation of many of the apparently capricious features of cholera epidemics; of, for example, its unequal diffusion in the endemic and epidemic area, of its sparing one house and attacking the next, of its sparing one side of a street and attacking the other side, and so forth. The circumstances of the water supply afford the explanation; one well or reservoir supplying a certain set of houses is contaminated, whilst that supplying neighbouring houses or districts is not. On the whole, low-lying districts are more subject to cholera than high and dry situations, overcrowded towns than sparsely populated districts, filthy cities than clean—facts entirely compatible with the water-borne theory of the disease.

If the proofs are fairly complete that the germs of cholera reside in the dejecta of the patient, they are equally complete that the mere fact of swallowing these germ-containing dejecta is not sufficient to convey the disease. Other conditions are necessary—conditions which include, apparently, a certain predisposition in the individual, and also certain epidemic conditions. The nature of these predisposing and epidemic conditions is quite unknown.

Koch, in 1883, separated from the stools of cholera patients in Egypt, and later, in 1884, in India, a special bacterium. This bacterium is now universally admitted to be present in the stools in practically all cases of cholera, and only in cholera. As a diagnostic indication, therefore, its presence or absence in the stools of patients suffering from choleraic symptoms is of great value. By many it is regarded not merely as a constant concomitant, but as the true germ of cholera. Its claims to be regarded as such are very strong indeed; nevertheless, being based principally on the fact of concurrence, these claims are not absolutely conclusive.

On account of its peculiar curved shape, the bacterium is sometimes known as the comma bacillus; sometimes it is called the cholera vibrio; sometimes the cholera spirillum. It is a very minute, actively moving organism, 1·5 to 2 μ in length by ·5 to ·6 μ in diameter, about half the length and twice the thickness of the tubercle bacillus. At one or both ends, at a certain period of its life, one or two flagella are discoverable on subjecting the cholera bacterium to special staining processes. These flagella are of great length—one to five times that of the bacterium itself. It is probable that it is to these flagella that the cholera vibrio owes its peculiar, active, spirillum-like movements. The bacillus can be cultivated in the ordinary culture media, especially if these are rendered slightly alkaline. It grows best at a temperatures of from 30° C. to 40° C., growth being arrested below 15° C. and above 42° C. Desiccation is said to kill it.

It liquefies gelatin; and in this as in various other culture media, it forms characteristic colonies. Although pathogenic to many of the lower animals, a powerful argument against attributing an etiological relationship to the comma bacillus in respect to cholera, lies in the fact that hitherto intentional experiment with these bacilli has never succeeded in producing in the lower animals, or in man, a disease having all the clinical features of the true epidemic disease.

Koch and others have succeeded in producing a disease in some respects like cholera, by introducing cultures of the bacillus into the intestinal canal of the guinea-pig, the contents of which had been rendered alkaline by carbonate of soda, and the peristaltic movements of which had been paralysed by opium. When the animals were killed, the intestine was found to contain a large quantity of cholera-like fluid and almost a pure culture of the bacillus, and to exhibit pathological changes closely resembling those of true cholera. Unfortunately for the claims of the comma bacillus, other micro-organisms have been found to give rise to similar effects. Buchner has suggested that, in addition to the comma bacillus, it is necessary for the production of true cholera to secure the presence of some other, and as yet unknown bacterium. He regards the disease cholera as the result of a mixed infection.

Morbid anatomy and pathology.—Rigor mortis sets in early, and lasts for a considerable time. Post-mortem muscular contraction sometimes causes curious movements of the limbs. If death has taken place during the algid stage, the body has a shrunken, shrivelled, livid appearance, and the tissues are all abnormally dry. Occasionally some of the muscles are found ruptured, doubtless from the violence of the cramps. The right heart and large veins are filled with dark, thick, and feebly coagulated blood, which tends to stick to and stain the inner surface of the vessels. Fibrinous clots may be found in the right heart and extending into the vessels. The lungs are dry, shrunken, and anæmic; sometimes they are congested and œdematous. The liver is congested, the gall bladder full, the spleen small. Like the other serous cavities, the peritoneum is dry and sticky. The outer surface of the bowel is generally injected and rosy-red in colour; the bowel itself contains abundance of the peculiar rice water material already referred to, and sometimes a little blood. The mucous surface is pinkish from general congestion, with spots or patches of an irregular and deeper congestion scattered about throughout its entire extent. Ecchymoses are common in the mucosa as well as in the serous membranes. The intestinal changes are most pronounced towards the lower end of the ileum, where Peyer's patches and the solitary glands are seen to be congested and swollen. In other instances the bowel may be pale throughout. Sometimes the mucous surface has a sodden, pulpy appearance, and exhibits exfoliation of epithelium; this is possibly a post-mortem change. Sometimes a diphtheritic exudation is met with towards the lower end of the ileum. The mesenteric glands are congested. The kidneys also are congested, the tubules filled with granular matter, and the epithelium cloudy, granular, or fatty and detached. The bladder is empty and contracted. If death have taken place during the stage of reaction, the tissues are moist; the venous system relatively empty; the lungs congested, œdematous, and perhaps inflamed; very probably there is also evidence of extensive enteritis.

The symptoms of cholera suggest a double action in the virus producing it. First, local irritation of the intestinal tract; second, poisoning through

the blood—phenomena which resemble those of ptomaine, mushroom, and similar forms of poisoning. The secondary fever of cholera is manifestly a reaction from the primary disease, complicated by inflammatory lesions the result of acute intestinal irritation.

Symptoms.—Cholera may supervene on what appeared to be an ordinary diarrhœa, and which, in view of the subsequent attack, is generally regarded as, and is called, "the premonitory diarrhœa"; or it may declare itself suddenly in the midst of apparent good health. When the disease has declared itself, the patient passes without pain enormous quantities of watery material. Stool follows stool in rapid succession. At first the discharges are fæcal in character; they soon lose their bilious colour, becoming like thin rice water in which small white flocculi are held in suspension. Vomiting of similar material generally supervenes. When the purging and vomiting have lasted a certain time—not necessarily a long time—cramps of an extremely painful description attack the muscles of the extremities, abdomen, and elsewhere, often causing the sufferer to cry out with pain. The patient now rapidly passes into a state of collapse, the surface of the body becoming cold and clammy—perhaps bedewed with sweat, the cheeks sunken, the features sharp and pinched, the eye sockets hollow, the fingers and toes shrivelled like a washerwoman's, the surface livid. The urine is suppressed; respiration becomes rapid and shallow, perhaps sighing; the breath cold, and the voice sunk to a hollow whisper. The pulse at the wrist rapidly becomes weak, flutters, and finally disappears. The patient is restless, tosses about complaining of intense thirst and of a burning sensation in the chest. The temperature of the surface sinks to 93° or 94° F. whilst that of the interior of the body, as indicated by the thermometer in the rectum, may rise to 101°, or even to 105°. Though occasionally he may wander slightly, the mind is usually clear. This, the algid stage of cholera, may terminate in death, in rapid convalescence, or in febrile reaction.

Death from collapse may occur any time from two to thirty hours from the commencement of the attack. Should, however, the vomiting and purging cease, the pulse may gradually return at the wrist, and the surface of the body become warm and dry. More or less febrile reaction then sets in. After some hours urine is again secreted, the slight febrile reaction subsides, and in a few days the patient may be perfectly well. On the other hand, on the cessation of the acute symptoms of the algid stage, febrile reaction may pass into a peculiar typhoid condition which continues from four to five days, or, in severe cases, even longer. The sunken cheeks and hollow eyes are now filled out and flushed, the tongue becomes brown and dry, and there may be low delirium with tremor and subsultus; or perhaps a peculiar torpid, apathetic condition may supervene. In this state the motions are greenish or like pea-soup; they may contain a certain amount of blood, and be very offensive. The reappearance of the urine in such cases may be delayed from two to six days. On its first appearance it is scanty, high coloured, cloudy, albuminous, and contains casts. Various complications, such as pneumonia, enteritis, asthenia, and uræmic troubles —as coma and convulsions—may prove fatal.

Such, briefly, are the principal clinical features of cholera. They may vary very much in severity and in the predominance of particular symptoms. Mild ambulatory cases occur; on the other hand, rapidly fatal cases of but three or four hours' duration are by no means rare. It is generally stated that the earlier cases in an epidemic are the most severe, and that those

occurring towards the end of an epidemic are milder. A fatal type of the disease is what is known as "cholera sicca." In such, although there is very little diarrhœa and vomiting, collapse sets in rapidly, the patient dying in a few hours without active purging or any attempt at reaction. In these cases, post-mortem examination discovers abundance of the characteristic rice water material in the intestine. Sometimes cases die suddenly from apnœa caused by coagula in the right heart, or, it is conjectured, by sudden spasm of the pulmonary arteries. Occasionally, after temporary improvement, relapse may set in and is nearly always fatal. Hyperpyrexia may supervene; it is rare, but when it does occur it is almost invariably fatal.

The sequelæ of cholera are various — anæmia, mental and physical debility, insomnia, irregular febrile conditions, chronic enterocolitis, different forms of pulmonary inflammation, ulceration of the cornea, gangrene, and so forth. Pregnant women almost invariably miscarry, the fœtus showing evidences of cholera.

Diagnosis.—Cholera resembles very closely many other diseases; among others, and especially, cholera nostras, acute diarrhœa, mushroom poisoning, ptomaine poisoning, some forms of malarial fever, the early stages of trichinosis. Diagnosis may be extremely difficult in sporadic cases; but during an epidemic of cholera acute purging of rice water stools can hardly fail to be the result of the virus producing the prevailing disease. A bacteriological examination may be necessary to establish the diagnosis. The absence of bile in the rice water stools, the vomiting of a similar material, the suppression of urine, the cramps, the cold shrivelled skin, the hollow whispering voice, and the prostration, taken together are fairly diagnostic. From algid types of pernicious malarial fever, a blood examination, in conjunction with the history of the case and the character of the prevailing epidemic, should suffice. It is well to note that in malarial choleraic diarrhœa a certain amount of bile is almost always present in the stools. The early stages of trichinosis may be inferred from the history of the case or cases, the discovery of adult trichinæ in the stools, and the subsequent history. Ptomaine and mushroom poisoning and cholera nostras may be diagnosed from a consideration of the concurrent circumstances, and the absence of the cholera vibrio from the stools.

Prognosis.—About half of those attacked with cholera die; in some epidemics, and especially at the early stage, the mortality is even greater. The young, the old, the weak, die more readily than the middle-aged and robust. Pregnancy, disease of the kidneys or of the liver, and dissipated habits, aggravate the mortality. As regards individual attacks, rapid progress, sudden seizure, extreme restlessness, rapidly failing pulse, intense algidity, hyperpyrexia, persistent suppression of urine, jaundice, lung and other complications, relapses of purging and vomiting, well-marked typhoid symptoms, uræmia, delirium, are all bad signs. In the algid stage, so long as the pulse can be felt at the wrist, and the temperature of the body is not exceedingly depressed, the prognosis is more hopeful. In the stage of reaction, in the absence of high temperature and of typhoid symptoms the prognosis is good. The return of bile in the stools, of the urinary secretion, of surface warmth, and of surface colour are good signs.

Treatment.—The prevention of cholera is to be sought for in domestic and municipal cleanliness, in a pure water supply, in isolation of the sick and destruction of their fomites by fire or disinfectants, in a rigid exclusion of the discharges from the water and food supply of the

community. Theoretically, strict quarantine should be an efficient safeguard; practically, it is not so. On the contrary, owing to the feeling of false security it engenders, it leads to neglect of sanitation. The modified quarantine, as practised in Great Britain, in which free pratique is given to all ships except those with cholera patients on board, together with careful sanitation, seems to be the most successful system for keeping the disease at bay. During epidemics of cholera, care should be taken to maintain the general health at a high standard, to avoid such things as may lead to derangement of the intestinal organs—uncooked fruit or vegetables, decomposing food of all sorts, excess in alcohol, purgative medicines—particularly salines—exposure, and fatigue. At these times water and milk ought to be boiled, and all cooking, eating, and drinking vessels washed in boiled water.

Haffkine has recently introduced a system of anticholera vaccination with the object of producing artificial immunity. His subcutaneous injections of cultures of the cholera vibrio have been extensively used in India; apparently they have met with a certain amount of success, sufficient at all events to justify further and more extended trial. On the assumption that the comma bacillus is the germ of cholera, they are correct in principle; they are thoroughly effective in the lower animals against poisoning by this microbe.

A vast number of drugs have been tried from time to time in the treatment of this disease; it cannot be said that much success has attended their use. Practically, the treatment of cholera resolves itself into careful nursing and the relief of suffering. Experience has shown that it is advisable by means of opium and other astringents to check diarrhœas during cholera epidemics; chlorodyne is perhaps the most generally used and most convenient form of administering opium. This, or, when vomiting is present, the hypodermic injection of morphine, together with rest, is probably the most valuable means of treatment at our disposal. Lead and opium pill, diarrhœa mixtures containing opium and carminatives, dilute sulphuric acid, etc., are also often used.

It is a mistake to attempt to feed or stimulate a patient, either during the premonitory diarrhœa or while active choleraic purging and vomiting are proceeding. At such times absorption is in abeyance, and food only adds to the derangement of the stomach and bowels. The intense thirst is best relieved by small quantities of ice or iced effervescing drinks; the cramps by small hypodermic injections of morphine and by gentle rubbing of the muscles, with or without a liniment. When vomiting has ceased, possibly a cautious use of iced champagne or of weak brandy and water may help to restore the circulation. The pulse can sometimes be brought back by nitrite of amyl inhalation; or, better, by intravenous injection of warm saline solutions—60 grs. of common salt, 30 grs. of carbonate of soda, to the quart of distilled sterilised water at a temperature of about 98°·4 F. The injection should be made by gravitation and slowly, at the rate of about a quart in a quarter of an hour, the effect being carefully watched; from one to three quarts may be required to restore the pulse. Sometimes this treatment has succeeded in saving life; usually, however, the improvement is but temporary, purging and vomiting rapidly removing the fluid injected.

It is of importance to maintain the temperature of the surface of the body. With this in view, the room must be kept at or over 70° F. Warm baths, or warm bricks or bottles may be placed about the patient,

who should be covered with a blanket, but not oppressed by too much clothing. The surface should be kept dry by frequent wiping.

During reaction, great care must be taken in feeding. Food should be given in small quantities—teaspoonfuls of milk every quarter of an hour, or teaspoonfuls of some meat jelly. If reaction is excessive and there is much fever, sponging of the surface or rectal injection of cold water may be tried. Dry cupping, hot fomentation, and poultices over the kidneys, and diluents may be had recourse to in persistent suppression of urine; everything like stimulating diuretics must be avoided. Constipation is best relieved by enemata; diarrhœa, by large enemata of solution of tannin.

During convalescence, tonics, change of air, and careful dieting are indicated.

<div align="right">PATRICK MANSON.</div>

DYSENTERY.

Syn., Fr., *Dysenterie;* Ger., *Ruhr.*

THE term "dysentery" is applied to a group of symptoms—tormina, tenesmus, and the frequent passage of scanty mucoid or muco-sanguinolent stools—depending on inflammation of the mucous membrane of the colon. It probably includes several etiologically distinct diseases.

History and geographical distribution.—Dysentery has been recognised from remotest antiquity. Galen attributed it to the irritating effects of an acrid bile; Sydenham regarded it as the local expression of a general disease; modern medicine inclines to look upon it as a purely local disease, resulting from invasion of the mucous membrane of the colon by one or more species of micro-organism.

Dysentery is found all over the world. Like malaria, its frequency and severity tend on the whole to increase as the equator is approached. It is unevenly distributed, some districts being more subject to it than others. It is endemic in many places, and, like malaria, is generally most prevalent in low-lying, damp localities. Unlike malaria, it has no exclusive predilection for the country, being nearly though not quite as common and often quite as severe in towns. Although sporadic cases and occasionally small and limited epidemics do occur in temperate climates, in them at the present day it is principally during war, in camps and sieges, during times of want, and in large public institutions—as jails or lunatic asylums—the subjects of grave sanitary defects, that this disease becomes extensively epidemic. Drainage, cultivation, improved water supply, improved food and sanitation generally, tend to repress dysentery; they have done much to banish it from Britain, where at one time this disease was common enough. In the tropics, sporadic cases are more numerous, and epidemics more frequent and extensive, owing, doubtless, to climatic causes, but partly also to the insanitary conditions so generally prevalent there.

Etiology.—The predisposing causes of dysentery include most influences that tend to cause congestion or debility of the alimentary canal—irritants of all sorts, bad food, insufficient food, purgatives, cold, sudden alternations of temperature, chronic congestion of the liver and stasis of the portal system, prolonged high temperature,

malarial fever, scurvy, constipation, damp, bad water—particularly if bad from fæcal contamination. overcrowding in unhygienic houses, intemperance, previous attacks.

There can be little doubt that there is a specific cause or causes at the root of the disease—a germ of some kind. What this may be has not been definitely settled. Recently Kartulis, Osler, Councilman and Lafleur, and others have put forward the *Amœba dysenteriæ*, whose connection with dysentery was first pointed out by Loesch in 1875, as the germ of at least one of the forms of this disease. There can be no doubt that this parasite and the disease are often found in association; and, further, that the amœba is often present, not only in the dysenteric discharges but also in the tissues constituting the base of the dysenteric ulcer, and also in the contents and walls of the frequently associated lesion—dysenteric abscess of the liver. But it is equally certain that the amœba is absent in many dysenteries and dysenteric liver abscesses; and, moreover, that it is often present in the healthy intestinal canal, and in the complete absence of dysentery. As yet the amœba has not been obtained in pure culture; consequently, it has been impossible to institute experiments on the production of dysentery by material from which all other germs had been excluded. It cannot, therefore, be said that the claims of the amœba have been scientifically established by the various experiments which have been made on the production of the diseases in cats and dogs by amœba-containing stools. The balance of opinion appears to be in favour of regarding the amœba as an epiphenomenon, the pre-existing inflamed condition of the intestine, and the abnormal nature of its contents favouring the multiplication of a parasite whose presence may aggravate lesions which in the first instance it did not produce.

Certain pathologists hold that the *B. coli commune* may acquire in some unknown way, possibly in consequence of the concurrent presence of another bacterium, pathogenic and transmissible qualities, and become a cause of dysentery. Ogata describes a minute bacillus in the dysentery of Japan. Durham has recently described another and still more minute bacterium in asylum dysentery. Others, again, regard the disease as a form of streptococcus infection.

In temperate latitudes, dysentery generally shows itself at the end of summer or beginning of autumn. In the tropics it may occur at any season, but most frequently about the end of the rains and the beginning of the dry season; that is, at a time when the fluctuations of temperature are most marked and most sudden.

Dysentery is not infectious in the ordinary sense; undoubtedly, however, some forms are communicable through the intestinal discharges, either in drinking water, or by direct contamination in common privies, or by being introduced into the bowel on instruments and so forth.

The incubation period has been stated at about from three to five days if infection have taken place by the mouth, at one day if by the rectum. Race has no special influence. Both sexes are equally liable. Children suffer often and severely. Occupation, unless in so far as it may entail special opportunities for infection, has no special influence. Pregnancy, childbirth, and miscarriage, if they do not predispose to dysentery, often very much aggravate it, and are always grave complications. A previous attack confers no immunity; on the contrary, it predisposes to recurrence.

Morbid anatomy.—The intestinal lesions in dysentery, although occasionally involving the last few feet of the ileum, are usually confined

to the large intestine, being most pronounced in the sigmoid flexure, or, though more rarely, in the cæcum; the transverse colon is usually less extensively involved. In the catarrhal form the mucosa and sub-mucosa are congested and œdematous, the surface softened, perhaps eroded and covered with a thick, tenacious, bloody mucus. In the ulcerative form there is a very great variety of lesion, including superficial erosions, small punched-out ulcers originating in inflammation and slough-ing of the solitary glands, and larger ulcers of various shapes and sizes. The latter originate from necrosing infiltration of the mucous membrane itself, from abscess formation in the submucosa, and from fistulous exten-sion in the latter producing sloughing. The part of the mucous membrane most affected is the edge of the transverse mucous folds. In gangrenous dysentery large areas of mucous membrane slough *en masse*, an entire circle of the bowel being sometimes involved. Dysenteric ulcers, as a rule, spare the muscular and serous coats; at times, however, these too are affected, adhesions to the neighbouring organs or perforation being the result. According to Councilman and Lafleur, in amœbic dysentery the elementary lesion is an abscess-like formation in the submucosa, con-taining thick gummy material and many amœbæ; subsequently the mucous membrane breaks down over this formation, thereby forming a character-istic ulcer.

In chronic dysentery the bowel is occupied by a larger or smaller number of chronic ulcers having thickened edges, and by areas of pig-mented scar tissue; it may be variously contracted and dilated in conse-quence of different degrees of narrowing and adhesion.

In acute dysentery the liver is generally congested, and, in tropical countries, is often (20 to 25 per cent.) the seat of one or many abscesses. The mesenteric glands are congested and swollen. In chronic dysentery the liver may be fatty or contracted; the kidneys may be the subject of some form of chronic nephritis; the mesenteric glands are hard and pigmented.

Symptoms.—It is customary to classify dysentery into acute and chronic. The acute may be subdivided into catarrhal, ulcerative, and gangrenous. In actual practice there is no hard-and-fast line of distinction between any of these various forms, one insensibly merging into the other. The individual cases during epidemics have a tendency to ap-proximate each other in type.

A dysenteric attack may commence suddenly, or it may supervene on what was regarded as simple diarrhœa. In the latter case the liquid motions gradually become less fæcal, more mucoid, and perhaps bloody; at the same time they increase in frequency, diminish in quantity, and become associated with griping and tenesmus. On the other hand, the symptoms of dysentery may suddenly supervene, generally during the night, without premonitory diarrhœa. When the disease is fairly established, the calls to stool are frequent or even incessant. Much pain, griping, and tenesmus attend the passage of small quantities of glairy mucus, which presently becomes tinged with blood. Straining to void these may be constant and extremely painful, and may be accom-panied with dysuria. Abdominal tenderness and distension may or may not be marked. Fever may be entirely absent; if present, it is usually of a very mild character, the thermometer rarely rising above 102° F. The tongue quickly becomes furred, and the appetite may or may not disappear. After a day or two the disease rapidly or slowly subsides; or it may

terminate in the more serious manifestations of the ulcerative or of the gangrenous form; or it may become chronic.

Should ulceration occur, the stools change in character; they are still mucoid and sanguinolent, but, in addition, they now contain larger or smaller flocculent masses of grey, sloughy-looking material, and stink abominably.

Should gangrene supervene, the stools become still more horribly fœtid, consisting principally of a material like flesh washings. Sometimes large sloughs, or even long tubes of gangrenous mucous membrane, are passed. The abdomen becomes exceedingly tender and distended. Vomiting and hiccough rapidly supervene, and, as a rule, death ensues within a short time.

When a catarrhal dysentery subsides, the stools gradually become fæcal, more copious and loose; finally the looseness subsides, and the patient may be quite well in the course of three or four days. When signs of ulceration develop, the case is necessarily more prolonged. Either form may merge into a chronic disease, in which the tormina and tenesmus, though diminished, do not completely subside. The stools become feculent, but they are rarely properly formed, generally containing mucus and often blood, their passage being attended with more or less griping and tenesmus. Sometimes, though the stools are formed, the surface of the mass is coated with mucus; sometimes they are partly formed, partly loose and mucoid; in other cases, they are liquid, feculent, and copious. This latter type of case is often mistaken for chronic diarrhœa. Sometimes constipation alternates with diarrhœa, or an apparently healthy motion is succeeded by one composed entirely of mucus and blood. Every now and again, in consequence of indiscretions in diet, of cold, of fatigue, or of other physiological error, a more acute relapse occurs. In this condition, sometimes better, sometimes worse, the case may go on for months or years, the general health becoming gradually undermined. Dyspeptic conditions, often accompanied by bare tongue or by superficial ulceration of the mouth, supervene. Intestinal atrophy, general wasting, œdema of the feet, and finally death, is too often the result in chronic dysentery. Chronic dysentery may not be of so urgent and fatal a character in every case, but at all times it is a grave disease.

Diagnosis.—Acute dysentery is easily recognised; the tenesmus, the character of the stools, and the history suffice in careful hands. In chronic dysentery, diagnosis may be more difficult; the possibility of hæmorrhoids, polypus, stricture, tuberculous, malignant, and specific disease, have to be taken into account. In this, as in all long-standing cases of intestinal flux, it is an excellent rule to make a digital examination.

Treatment.—Rest in bed and diet are the most important matters in the treatment of acute dysentery. Food should be given in small quantities; it must be of a digestible character and of a kind calculated to produce a small fæcal residuum. Milk, thin chicken-tea, egg-albumin water, thin barley water or rice water, are the best foods during the acute stage. They should be given in small quantities at a time, and neither hot nor cold.

There are three principal plans of drug treatment in dysentery— ipecacuanha, the purgative sulphates, and calomel.

Ipecacuanha is best given somewhat as follows:—The patient must abstain from food and drink for at least three hours. Twenty drops of laudanum are then given, and a mustard poultice applied to the epigastrium. About twenty minutes later, 20 to 30 grs. of powdered ipecacu-

anha root, either in bolus or in a small quantity of water, is administered. The patient must then lie flat on his back without a pillow, and endeavour to avoid vomiting; he may neither eat, drink, speak, nor move for three or four hours. If vomiting occur soon after the powder is given, in an hour or two a second may be administered. After three or four hours, small quantities of food may be given during the succeeding six or eight hours, when the drugging is to be repeated. Guided by its effect, the use of ipecacuanha is kept up for two or three days. A great drawback to this treatment is the severe vomiting which sometimes ensues; but, notwithstanding this drawback, there can be no question of its value in some cases, although in others it appears to do little or no good. If the ipecacuanha produce a large, loose, bright yellow stool, improvement is nearly sure to follow.

The sulphates, preferably the sulphate of soda, may be given either in drachm doses every quarter of an hour, or in half-ounce doses every hour, until a loose feculent motion is produced. The drug should be continued, and so administered as to secure two or three copious loose motions daily.

Calomel is given either in 5-gr. doses every six or eight hours, or in smaller fractional doses of a quarter to half a grain every hour for a short time; it may be combined with opium or with ipecacuanha.

So soon as the stools become feculent and free from mucus and blood, a mixture of bismuth salicylate, 15 grs., and liquor morphinæ, 5 to 10 minims, in mucilage and water, should be given and continued until the motions become solid. Tenesmus is best relieved by a small enema of laudanum, 30 to 40 drops in 2 oz. of starch. Washing out the rectum with hot boracic water is sometimes successful. Hot baths and hot fomentations to the abdomen, at times prove useful.

Chronic dysentery requires very careful dieting, and often great variety of therapeutical treatment. Amongst many measures adopted may be mentioned a pure milk diet, a meat juice diet, a mixed diet, a dry diet. Fruit juices or vegetables ought always to enter into the dietary of long-standing cases. Small doses of castor-oil; small doses of ipecacuanha; calomel, opium, and ipecacuanha pill, 1 gr. of each; strong decoction of simaruba; castor-oil alternating with opium; 20-drop doses of turpentine; massive (40 oz.) injections of nitrate of silver—half to one grain to the ounce; injections of alum, of salicylic acid, of tannin, of boracic acid, of cold water, are some of the measures that have been employed with more or less success. A sea voyage is often of great value. A course of Carlsbad water is also beneficial at times. Clothing ought always to be warm. Alcohol, as a rule, is badly borne and aggravates the condition. Exacerbations should be treated with ipecacuanha, the sulphates, or calomel. In the tropics the subjects of chronic dysentery should be sent to a dry, temperate climate. The winter and spring months in England do not, as a rule, suit those cases; at that season they should remove to some milder, drier climate.

<div style="text-align:right">PATRICK MANSON.</div>

LIVER ABSCESS OF WARM CLIMATES.

A FORM of suppuration occurring in the liver, especially in warm climates, and almost invariably as a sequel to dysentery. It is rarely

idiopathic, and still more rarely a result of the dysentery of temperate or cold climates.

History and geographical distribution.—Abscess of the liver has been recognised since the remotest times. Its connection with dysentery was indicated by Twining and Annesley in the earlier part of the present century. The probability of its being caused by morbid material conveyed to the liver from dysenteric conditions of the colon by the portal vein, was first distinctly formulated by Budd. The latest important addition to our knowledge of liver abscess was made, not many years ago, by Kartulis in Egypt, who was the first to indicate the occurrence of *Amœba coli* in the characteristic pus.

The geographical range of this disease is regulated by that of dysentery; in the tropics, where dysentery is prevalent, there, as a rule, liver abscess is proportionately common. There can be no question of the intimate association of the two diseases, but the frequency of this association is not invariably, nor everywhere, nor at all times the same. Some epidemics of dysentery lead more frequently to liver abscess than others, and the dysentery of some districts is more liable to this complication than that of others. A close study of the relative geographical distributions of the two diseases shows that whilst in many parts of Asia and Africa the greater the prevalence of dysentery the more frequent the occurrence of liver abscess, in other places, as in the West Indies, it is not so. In the West Indies, although dysentery is common enough, liver abscess is relatively rare. Similarly in temperate climates, as a sequela of dysentery contracted in these climates, liver abscess is almost unknown. One or two epidemics in temperate climates have been associated with a certain proportion of cases of liver abscess; but, as a rule, in this country dysentery, which is a common disease at times in many of our lunatic asylums, and which has more than once been epidemic in some of our jails, is not so followed. In India, post-mortem examination has shown that about one-fifth of the Europeans who die of dysentery in that country are the subjects at the same time of liver abscess. The geographical ranges of liver abscess and dysentery concur, therefore, only in warm climates, and in them only to the extent that liver abscess is rare or unknown in places where dysentery is rare or absent.

Etiology.—Presumably the real cause of liver abscess, as of abscess elsewhere, is a micro-organism of some sort. Although many micro-organisms—staphylococci, streptococci, *B. coli communis,* and other bacteria—have been found in the pus, in the majority of instances the usual pyogenic micro-organisms are absent. According to my experience, *Amœba coli* is present in more than half the cases of tropical abscess seen in England; in Egypt, according to Kartulis and others, the association is still more frequent. A proportion of liver abscesses contain neither bacteria nor protozoa; possibly, though present at one time, they had subsequently died out. Although the frequent presence of these organisms in liver abscess is undeniable, in view of their occasional absence, it cannot be said that we understand their exact relationship to the disease.

The adult male European in tropical countries is the principal victim of liver abscess. Natives, and European women and children, are much more rarely attacked. The reason for this difference in liability is not very obvious; for, in the tropics, dysentery, assuming it to be the cause of liver abscess, is quite as common in natives and in European women and children as it is in the European male adult. It is generally supposed that

the superabundance of rich food and alconolic drink consumed by many European male adults in the tropics is the cause of their superior liability to liver abscess. It is conjectured that in warm climates conditions of hepatic congestion are specially liable to ensue from such indulgence, and that the normal resisting powers of the liver to any organism or morbid product that may be carried to it by the portal vein from a dysenteric colon is thereby impaired. There are two facts which support the idea that imprudence in eating and drinking have something to do with the causation of liver abscess—first, natives who adopt European habits as regards eating and drinking acquire an enhanced liability to liver abscess; second, liver abscess is comparatively rare in total abstainers. It is evident, however, that other elements must enter into the etiological nexus; otherwise, how explain the comparative rarity of liver abscess in the West Indies, where high living is often enough combined with the tropical heat and dysentery.

Recent writers declare that cases of liver abscess of apparently idiopathic origin are attributable to an actual, though symptomatically latent dysentery. Others have thrown out the idea that both the liver disease and the disease of the colon are independent consequences of the same cause. They point to cases in which hepatitis seemed to have preceded dysentery, and to other cases in which attacks of dysentery and of hepatitis alternated. For myself, I have not yet seen a case of tropical liver abscess in which a history of dysentery could not be elicited. It should be borne in mind that dysentery is very often wrongly diagnosed as diarrhœa, and also that it may be entirely overlooked.

In temperate climates, apart from those suppurations of the liver occurring in pyæmic conditions, in disease of the bowel and of the gall bladder, in hydatids and in other parasitic affections, what appears to be idiopathic abscess does occasionally occur.

Liver abscess occurs principally between the ages of 20 and 40. It is more common during the first three or four years of tropical residence than subsequently. On the other hand, it may not declare itself until after years of tropical life; sometimes not until the patient has returned to his native temperate climate. Chills, excesses, local violence—as a blow, but particularly chills—seem at times to have a marked influence in determining suppuration in the liver of those predisposed to its occurrence by an existing or pre-existing dysentery.

Morbid anatomy.—At a stage preceding the actual formation of liver abscess, there is usually to be found general congestion and enlargement of the organ. On section, one or more greyish anæmic patches from quarter to one inch or more in diameter, having ill-defined borders, and with the centre tending to soften, are discovered. If these grey patches are pressed, a drop or two of gummy purulent material may be expressed. Later, the centre of the patch breaks down, and a cavity containing the characteristic chocolate-brown, viscid purulage is formed. This cavity increases by degrees, partly by molecular disintegration of its rough, ragged, irregular wall, partly by the falling into it of considerable masses of necrotic tissue. One or more abscesses may coalesce. There is no proper abscess wall; there is a zone of surrounding congestion, but there is little, if any, inflammatory infiltration. There may be only one abscess, or there may be two or three, or a very large number (multiple abscess of the liver). The individual abscesses vary in size from an insignificant cavity to one of many ounces capacity, a whole lobe or even the entire organ being,

perhaps, converted into a huge pus sac. When the abscess becomes encysted (a rare event), the wall of the sac is converted into a thick, tough, fibrous membrane which completely shuts off the cavity from the rest of the organ. In time the fluid part of the contents may be absorbed, a cretaceous or cheesy mass remaining. When liver abscess approaches the surface of the gland, the implicated peritoneal surfaces inflame and generally become adherent.

Symptoms.—These vary very much both in character and intensity. As a rule, at the commencement they do not appear to be proportionate to the importance of the organ involved or to the gravity of the disease. In some cases the oncoming of abscess is attended with all the signs of suddenly developed, acute inflammation, or congestion of the liver. In such there may be stabbing pain in the right side in the region of the liver. The pain is greatly aggravated by the movements of respiration, by coughing, sneezing, and the like. There is a sense of weight and fulness in the right hypochondrium; possibly there is severe pain or aching in the right shoulder; often there is a short, dry cough. The tongue is foul; anorexia is complete; fever may run high. On examination, it will be found usually that the respiratory movements on the affected side are restricted, the right rectus tense, and perhaps the corresponding leg drawn up. Firm palpation and percussion over the liver give great pain. There is general increase in the size of the organ both upwards, downwards, and transversely. With or without the occurrence of rigor, which may be very violent, the fever gradually merges into the hectic type, temperature being normal, or nearly so, in the early part of the day, and high—102° to 103°—in the evening. Profuse sweating now occurs, especially during the night, or whenever the patient falls asleep. Bulging of some part of the hepatic area may develop and be apparent to the eye, or ascertainable by percussion or palpation. The patient, as a rule, lies on his back or on his right side; in some rare instances he may rest more comfortably on his left side.

In other and in the majority of cases there may be no such dramatic commencement of the disease, the patient not being able to say exactly when his disease began. He gradually loses health; is languid; suffers from anorexia; has a foul tongue; has constipated or irregular bowels; sometimes he may vomit or show other symptoms of gastric and intestinal catarrh. He may or he may not have pain and sense of weight or fulness about the liver. If the thermometer be used, it will be found that temperature rises towards evening to 101° or 102°, the rise being sometimes preceded by slight or more marked shivering. Profuse sweating during the night is nearly a constant occurrence. On examination, the liver is found enlarged, although not necessarily to a very great extent; the enlargement may be general or it may be localised.

When abscess has formed, the following symptoms—some or all of them —are generally to be found:—A low morning and high evening (101°- 103°) temperature; profuse nocturnal sweating; a rapid, feeble pulse; wasting; generally a foul tongue; anorexia; a muddy complexion; languor; sleeplessness; great depression of spirits, and usually irritability of temper. Locally we may find enlargement of the liver; tenderness at one or more points; fulness of the right side and epigastrium; obliteration of one or more intercostal spaces; perhaps a rounded swelling. To these are sometimes added dry cough, rigid right rectus muscle, pain in the right shoulder, dorsal or right-side decubitus, very rarely jaundice or splenic enlargement.

As the disease advances the symptoms become more definite, wasting is progressive, debility extreme. There may be œdema of the feet, diarrhœa, etc. If not relieved by surgical means, the case terminates either in death from exhaustion, or in rupture of the abscess through the lung, the characteristic chocolate-coloured viscid pus, mixed with blood, being expectorated; or into the pleura, the stomach, the intestine, the peritoneal cavity, or externally. In a very few instances liver abscess has burst into the pericardium, gall ducts, pelvis of the right kidney, into the vena cava, or other large vessel. Occasionally the abscess becomes encysted; in this event constitutional symptoms subside, and the patient recovers.

When rupture takes place into the right lung, the most frequent direction, there may be a sudden gush of pus which floods the bronchial tubes and almost suffocates the patient; or the contents of the abscess may be coughed up more gradually. In either event, in about half of these cases, recovery, rapidly or more slowly, ensues. On the other hand, hectic symptoms may continue, and, after weeks or months, a certain amount of pus being brought up daily, or at intervals, the patient succumbs from slow exhaustion. When rupture takes place into the right pleura, the physical symptoms of pleuritic effusion are rapidly developed. When rupture occurs into the stomach, the escaping pus may be got rid of by vomiting; if into the bowel, it may be voided as a diarrhœa-like motion.

Diagnosis.—This rests principally on the following points:— (1) Residence, present or past, in a tropical climate; (2) a history of dysentery; (3) the occurrence of a more or less distinct evening rise of temperature; (4) enlargement of the liver; (5) pain or discomfort in this organ. Such an assemblage justifies a suspicion of abscess. If bulging of one or more intercostal spaces, tenderness on pressure over a particular spot, friction (pleuritic or peritoneal), or a limited and rounded swelling continuous with the liver dulness; if all or any of these are present, the diagnosis of liver abscess is so likely to be correct that exploratory aspiration, with a view of confirming or possibly refuting it, should be had recourse to. In all cases in which liver abscess is strongly suspected, exploration with the aspirator should be practised with as little delay as possible, the surgeon being prepared to operate at once if pus is found. Exploration should be made under chloroform. The point selected for entering the needle may be indicated by swelling, tenderness, or fixed pain. Failing such a guide, a point in an intercostal space close to the edge of the ribs and slightly in advance of the midaxillary line should be selected. The exploring needle, which must not be too small, should be thrust inwards and somewhat upwards, and to its full extent if pus is not found nearer the surface. If the abscess be not struck, there should be no hesitation in re-entering the needle at various points of the area of dulness. If necessary, every part of the organ should be freely explored, as far as anatomical considerations render it practicable. There is little danger attending this operation; there is much greater danger in neglecting or postponing it. As a guide, the fact that the majority of liver abscesses occur in the upper and back part of the right lobe, has to be borne in mind.

The fever attending liver abscess is often mistaken for malarial intermittent; but the history of the case, the absence of considerable splenic enlargement, the absence of the plasmodium from the blood, and the uselessness of quinine, should obviate this mistake. Syphilitic disease of

the liver, leucocythæmia, pernicious anæmia, gallstones, suppurating hydatids, may each be attended with fever and enlargement of the liver, and require to be considered in attempting diagnosis. It sometimes happens that the pleuritic and pneumonic symptoms which affect the base of the right lung in suppurating hepatitis, and which so often precede rupture of an abscess through the lung, are misinterpreted, and the attendant liver abscess ignored. Such an error can best be avoided by careful inquiry into the history, and careful physical examination. A history of antecedent dysentery, followed after a variable time by hectic fever and subjective and objective symptoms referable to the right side generally, indicate, almost invariably, abscess of the liver.

Prognosis.—In simple abscess of the liver, which has been operated on early, the prognosis is good. In multiple abscess, which is generally to be suspected if fever does not subside after free drainage, prognosis is bad. Spontaneous opening of abscess through the skin or lung leads to recovery in about half the cases. Rupture into the alimentary canal is not so favourable; if into the peritoneum, pericardium, or into a blood vessel, it is almost necessarily fatal.

Treatment.—When hepatitis declares itself, and before suppuration has taken place, the patient should be sent to bed, placed on very low slop diet, and freely purged with sulphate of soda. Sometimes a full dose of ipecacuanha, as in dysentery, is useful. At the same time, large hot poultices should be laid over the region of the liver and frequently renewed. If it is believed that suppuration has occurred, the liver must be explored at once; if an abscess is struck, it should be opened and thoroughly drained. Diet must now be more nutritious; at the same time it should be unstimulating. Aspiration often does much good, even if no abscess is discovered, a fact which encourages its early employment. If temperature does not fall within a few days of opening an abscess, and if drainage be satisfactory, a second abscess may be suspected, and should be sought for.

If, after rupture into the lung or elsewhere, the patient remain hectic and continue to lose flesh, and whether he is or is not expectorating pus, an attempt should be made to reach and drain the abscess from the outside. Not unfrequently in such cases a subsidiary abscess forms above the diaphragm through which, by means of a small sinus, it communicates with the original abscess in the liver; if feasible, this pulmonary abscess should be drained.

PATRICK MANSON

MEDITERRANEAN FEVER.

A SPECIFIC fever occurring on the shores of the Mediterranean, and possibly elsewhere. It is characterised by a long and indefinite course of several weeks' or months' duration, made up usually of alternating waves of exacerbations and remissions, profuse perspirations, anæmia, liability to rheumatic-like affection of the joints, neuralgia, orchitis, etc., and distinguished pathologically by the presence of a specific microorganism in a somewhat enlarged spleen.

History and geographical distribution.—For many years this disease was confounded both with enteric and with malarial fever. Marston, in 1861, was the first to recognise its special nature, and to

correctly describe its clinical features. In 1887, Bruce established its specific character by demonstrating its dependence on a bacterium—*Micrococcus melitensis.*

So far as is definitely known, the disease is confined to the Mediterranean ports, where it passes by a variety of local names, of which Malta fever and Rock (Gibraltar) fever are best known to English readers. Possibly the same disease occurs on the shores of the Red Sea, in India, the West Indies, and elsewhere in the tropics and sub-tropics. It is one of the most frequent causes of invaliding in the garrisons at Malta and Gibraltar.

Etiology.—Mediterranean fever is not directly communicated from person to person. In Malta and Gibraltar its prevalence is found to be in inverse ratio to the monthly rainfall, occurring mostly during the dry hot weather from May to September, and being most common in dry years. The water and food supply have no manifest influence. The infection is generally believed to be air-borne, and to proceed from sewage-saturated foci. Certain spots, owing to their proximity to certain drains, are specially infective.

From 15 to 40 is the most susceptible age. Women are more liable than men. All conditions of life are subject to the disease. Length of residence has no immunising effect. It is probable that one attack confers a temporary, but not an absolute or permanent protection.

Careful bacteriological studies by Bruce, Gipps, Hughes, and Wright make it in the highest degree probable that this disease is the result of invasion of the spleen by the bacterium already referred to. The *M. melitensis* can be cultivated and isolated. On injection of a pure culture into a monkey, fever—similar to that occurring in man—ensues. The bacterium can be recovered from the monkey and recultivated; on subsequent injection into a second monkey it will again produce the disease.

Morbid anatomy.—Hughes reports that in sixty post-mortem examinations, pulmonary congestion, generally with pneumonic consolidation and with injection of the bronchi, was present in 87 per cent. The heart is pale and flabby. Patchy congestion—not involving Peyer's patches—and, though less frequently, a peculiar œdematous swelling of the intestinal mucosa, occur in the majority of cases. The liver may be congested. The spleen is always enlarged, congested, soft, friable, often diffluent, and weighs from 15 to 19 oz. The kidneys are also congested. The microscopical appearances of the various organs are such as may be expected in any case of severe and protracted fever.

Symptomatology.—Hughes, who writes from an experience of upwards of one thousand cases, after remarking on the variability of the symptoms, and after putting aside the milder and indefinite cases, classifies the types of Mediterranean fever into undulatory, intermittent, malignant.

The undulatory type.—In this there is a gradual step-like rise of temperature until 104° or 105° F. is attained, with slight morning remissions and evening exacerbations, together with increasing gastric symptoms, constipation, general pains, and headache. Some pulmonary congestion or catarrh now shows itself. After a week or longer the fever and other symptoms begin to abate in the same gradual manner as they arose, the daily remissions being accompanied by profuse sweats. When temperature has been normal, or nearly so, for a few days, the gradual step-like rise of temperature and gradual step-like fall, accompanied by the same symptoms,

are repeated. Relapse again occurs; and so on, in a succession of alternating waves of fever and apyrexia, the disease continuing for an indefinite period of weeks or months. The length of one of the constituent waves varies from one to five weeks, the average being about ten days. The recurring relapses tend to become progressively shorter and milder; anæmia and wasting advance, however, and may reach a high degree. The more general symptoms are often associated with neuralgia of various nerves, often with sudden effusions of a metastatic and fleeting nature into various joints, with orchitis, bronchial catarrh, lobular pneumonia, palpitations, rheumatic and other complications. After two or three months, temperature becomes permanently normal, and then slow convalescence, easily interrupted, sets in. The average duration of the disease from first to last is from sixty to seventy days; but it may be very much longer, sometimes a year or even more.

The intermittent type.—In this the daily fluctuations of temperature are more marked, the chart being like that of hectic; at the same time a tendency to waves of increase and decrease of pyrexia, and a liability to similar complications as in the undulatory type, are observable.

The malignant type.—The patient, after four or five days of rapidly intensifying severe febrile distress, with well-marked gastric and intestinal disturbances, slight splenic enlargement, hepatic and epigastric tenderness, diarrhœa, and a temperature of from 104° to 107° F., shows pronounced signs of pulmonary congestion and general bronchitis. Later, the fever continuing, the tongue dries, the mind becomes clouded, and the typhoid state is established. Fatal hyperpyrexia (110° to 115° F.) may then develop, or cardiac failure may occur, the patient dying any time during the first (13·7 per cent.), second (18·3 per cent.), third (25 per cent.), or fourth week, or even later. There may be one or more temporary abatements of fever, as in the preceding types, with subsequent and fatal relapse.

Special symptoms of more or less frequent occurrence are desquamation, most noticeable on the soles of the feet, occurring about the fourth week; falling of the hair, especially in protracted attacks; slight bronzing of skin; a peculiar odour emitted by the patient's body; profuseness of diaphoresis, particularly marked in the intermittent cases; presence of pronounced rigors; the anæmia; œdema of ankles during convalescence; absence of organisms in the general circulation; slight but distinct swelling of the spleen; slighter or graver pulmonary complications in about 95 per cent. of cases; occasionally pleurisy; gastric symptoms such as anorexia, foul tongue, epigastric tenderness; constipation (81 per cent.); diarrhœa (4 per cent); occasionally epistaxis.

Among the symptoms referable to the nervous system, headache and shifting pains in back and limbs are prominent during the early stages. Later, there may be facial or occipital neuralgia, lumbago, sciatica, intercostal neuralgia, cutaneous hyperæsthesia (especially of the soles), insomnia, delirium, and other mental disturbances, and occasionally though rarely paresis with atrophy of certain muscles.

Joint effusions, especially in the rheumatic, are a common characteristic during or after the third week. They may come and go suddenly, and are attended with great pain; redness of the part is uncommon. These effusions do not eventuate in ankylosis. Acute epididymitis and orchitis occasionally supervene.

Diagnosis.—This is often a matter of great difficulty; typhoid fever,

malaria, rheumatic fever, tuberculosis, and septic conditions being all more or less simulated by this disease. The occurrence of alternating pyrexial and apyrexial waves, of profuse diaphoresis, of the rheumatic-like affection of joints; together with absence of rash, of diarrhœa, of dry tongue, of hæmorrhages, of typhoid serum reaction, and of Ehrlich's rose-red urine reaction, and considerations of season and place, should aid in the diagnosis from typhoid.[1] Malaria is more easily excluded by a microscopical examination of the blood and by the quinine test; rheumatic fever by the impotence of the salicylates; tuberculosis by the absence of the bacillus; septic conditions by the absence of evidence of septic foci such as ulcerative endocarditis, abscess in the liver, or pus formation elsewhere.

Prognosis.—Considering the length and severity of the disease, the danger to life is small. The mortality in those attacked is under two per cent. So far as invaliding is concerned, the prognosis is not favourable, ninety days being the average time on the sick list. Complications, but particularly a tendency to hyperpyrexia, should lead to a very guarded prognosis.

Treatment.—Prophylactic measures should be based on the fæcal origin, and on the air-borne character of the virus. They must therefore include avoidance of soil pollution, a perfect system of drainage, efficient sewer ventilation, and abundant flushing with water. As a precautionary measure, Mediterranean towns should be avoided, if possible, from June to October—the season of greatest prevalence of Mediterranean fever.

The treatment of this disease is more a matter of nursing, feeding, and patience than of drugs; there is no specific. As a primary and essential measure, the patient should be removed from the spot in which the disease was contracted. He ought to be confined to bed and placed on a fluid diet, of which milk and, in the absence of diarrhœa, animal broths are the more important elements. Fruit juices, as freshly-made lemonade, should always be prescribed: this measure has to be specially attended to, since in the absence of all vegetables from a dietary which may have to be adhered to for several consecutive months, scorbutus might very well ensue. In view of the profuse sweating and consequent liability to chill, the patient should sleep in flannel. Constipation may be treated by enemata or by mild aperients; diarrhœa, if present, by avoiding animal broths and by the use of small quantities of opium or other astringents. Stimulants may have to be given; unless definitely indicated, they are, perhaps, better avoided. Sleeplessness may require opiates, sulphonal or bromides; headache yields to antipyrine. This last drug, in view of its depressing effect, must be used with caution, particularly in the later stages of the disease, when there is much cardiac debility. Swollen and painful joints indicate hot fomentations, belladonna applications, and wrapping in cotton-wool. If temperature runs high—above 103°—tepid or cold sponging may be used; if there be actual hyperpyrexia, the cold bath must be employed promptly and thoroughly.

Return to ordinary diet may be attempted only when the tongue is clean; even then the resumption of solid food should be made with the greatest care. Tonics, wine, beer, and change of air are useful during convalescence. Quinine does harm in the early stages; later, in small doses,

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[1] Wright and Semple state that the blood serum in Mediterranean fever gives a characteristic clumping reaction with cultures of *M. melitensis*, an observation which more recent experience has confirmed.

it is beneficial as a stomachic and tonic. The anæmia indicates iron and arsenic.

During autumn and winter, it is not advisable to send patients home to the cold of England; if the return can be made in summer, it is to be advised, provided in other respects the patient is able for the journey.

PATRICK MANSON.

SPRUE.

A DISEASE of warm climates, characterised by irregular action of the bowels; profuse fluid or pultaceous, pale, frothy stools; flatulent dyspepsia; and, very generally, a raw, eroded condition of the mucous membrane of the tongue, mouth, and gullet. It runs a chronic course; is subject to exacerbations and remissions; and, if unchecked, terminates in atrophy of the gastric and intestinal mucosa, general wasting, and death.

History and geographical distribution.—The type of case which in recent years has come to bear the name "sprue," was more or less clearly recognised by the earlier writers on tropical diseases, being described by them as " tropical diarrhœa," or under some such indefinite and perhaps misleading term; but it is only recently that this disease has attracted much attention, and been recognised as possessing characters of a kind more or less specific. It is probable that sprue exists in all tropical and sub-tropical climates. Although the first clear description of the disease (Hillary's) applied to the West Indies, it is principally from China, the Eastern Peninsula, the islands of the Eastern Archipelago, and from India that modern accounts emanate.

Etiology.—The specific cause, if such exist, is unknown. The principal predisposing cause is undoubtedly residence, particularly, though not necessarily prolonged, residence in a tropical or subtropical climate. Sprue is apt to supervene on dysentery, diarrhœa (especially the morning diarrhœa of the tropics), prolonged lactation, frequently-recurring preg-nancies, miscarriage, uterine hæmorrhages, malarial fevers, and other causes of debility, especially those associated with disease of the alimentary canal. In some instances, apart from tropical residence, neither predispos-ing nor exciting cause can be traced. Although residence at some time in a warm climate is a necessary condition, the disease may not declare itself until the patient has returned to the temperate zone.

Both sexes are liable. Sprue is not reported as occurring in children. It is rare in natives, being principally confined to Europeans. Rich and poor, temperate and intemperate, are alike liable.

Morbid anatomy and pathology.—Post-mortem, the aliment-ary canal is found so thinned as to be almost diaphanous. A viscid, dirty grey mucus coats its inner surface. When this is washed away, points, patches, and large areas of injection and erosion are seen in the subjacent mucous membrane. The villi, follicles, and glands in many places are atrophied or completely destroyed. Small pigmented cicatricial patches may be visible here and there. On microscopical examination of sections, besides the destruction of villi and glands, fibrotic changes in the submucosa are usually very manifest. The œsophagus may be implicated as well as the stomach and intestine. Sometimes deeper ulceration is met with, especially in the lower part of the ileum and in the great intestine.

Inflammation, as well as degenerative changes in the acini of the pancreas, have been reported. Beyond these, and general dryness and wasting of all the tissues of the body, there appears to be no other lesion peculiar to sprue.

In the absence of all knowledge as to the special cause of this disease, we must regard sprue as the result of some incapacity of the European constitution to withstand tropical climates and morbid influences, parasitic or other, occurring there—an unsuitability which renders the European prone to a chronic form of gastro-intestinal catarrh, and possibly to exhaustion of the glandular structures appertaining to the digestive system. The absence of bile from the stools, and the enormous bulk of the latter, suggest that in some way the intestinal and digestive juices are deficient, as if from exhaustion of the glands. Very probably the decomposition of undigested food has something to do with the irritative lesions which are so prominent a feature at post-mortem examinations.

Symptoms.—The subject of sprue generally gives a history of gradually increasing diarrhœa. In a few instances the onset may be more sudden. As a rule, however, at first the diarrhœa occurs only in the morning and forenoon, the two or three loose and somewhat copious stools which are then passed being, perhaps, for a time bilious in character. By degrees, or more suddenly, the motions become more numerous, more profuse, and are now observed to be singularly pale, frothy, and fermenting, sometimes pultaceous, always strikingly excessive in amount. At the same time, dyspeptic distension, especially after food, is troublesome, and there is developed a characteristic inflamed condition of the mouth and pharynx.

The disease is subject to exacerbation and remission; rarely is it altogether in abeyance. During the exacerbations the mucous membrane of the tongue, of the floor of the mouth, of the cheeks and lips (particularly where they are in contact with the teeth), and of the palate and pharynx, is seen to be congested and raw-looking, the edges of the tongue being thrown into transverse folds. Here and there eroded patches, sometimes minute, sometimes more extensive, often covered with a viscid coating of muco-pus, are discoverable. The whole of the mouth is exquisitely sensitive, so that only the very blandest foods can be taken. Owing to the attendant irritation, a large quantity of saliva is secreted, and is continually being swallowed, or, when swallowing is very painful, being allowed to dribble from the corners of the mouth. From time to time this acute phase subsides, and then the tongue is seen to be if anything rather small; it is clean, bare, apparently devoid of fur and papillæ, and glossy as if covered with thin varnish. Though less sensitive in this condition than when eroded, it is still over-sensitive. During the exacerbations especially, and doubtless in consequence of a similarly inflamed eroded condition of the pharynx and œsophagus, swallowing is painful; and there may be also a sense of heat or rawness under the sternum. Vomiting, without much nausea, is not an unusual occurrence.

By degrees the patient loses weight, becomes anæmic, irritable, and weak both mentally and physically. The skin acquires a dark, muddy, dry, lustreless appearance, and hangs in loose folds on the wasted body and limbs. The liver partakes in the general wasting, yielding only a narrow percussion area suggestive of cirrhosis. From time to time, as the disease advances, the patient may be confined to the house, or even to bed, from the urgency of the diarrhœa and attendant prostration. Cold—especially cold and damp—or very hot weather, mental worry, or the slightest

indiscretion in food, aggravate all the symptoms. In this way the case goes on for months and years; one month a little better, the next a little worse; on the whole losing ground. Finally, unless properly treated, and treated at a sufficiently early stage, the patient dies either from some intercurrent disease, from sudden profuse diarrhœa, or from exhaustion; in the latter case œdema of the feet and legs usually preceding the fatal event.

With care sprue may remain in abeyance for years, relapse and recovery alternating from time to time. In some cases, under treatment, diarrhœa and sore mouth subside, but the stools continue amazingly excessive in quantity and devoid of colour; such cases, notwithstanding the cessation of diarrhœa, die. Minor degrees of sprue are also seen, in which a liability to sore mouth and morning diarrhœa of pale stools may continue for years, without, apparently, seriously impairing the general health.

Diagnosis.—The peculiar condition of the mucous membrane of the mouth, the pale, fermenting, and strikingly copious stools, the wasting, and the history of residence in the tropics, suffice to establish a diagnosis of sprue.

Treatment.—The most efficient treatment for this disease is undoubtedly a diet exclusively of milk. To be successful, the diet should be of the most stringent character, and persisted in for many weeks, or even months. The patient, if seriously ill, should be sent to bed in a warm room and warmly clothed. At first the daily quantity of milk, which in cold weather must be slightly warmed, should not exceed 60 oz. It should be taken in divided quantities at intervals of an hour; it must be sipped, and not drunk. If the treatment is to prove successful, in a few days the motions become solid, the dyspeptic distension disappears, and the condition of the mouth rapidly improves. The quantity of milk may now be increased gradually until six or eight pints are taken in the twenty-four hours; this must be continued for at least six weeks. If all signs of the disease have disappeared, other food may be carefully added; at first, raw eggs, thin broths; then, after a time, chicken, farinaceous foods thoroughly cooked; and, finally, underdone lean of meat. When bread is introduced, it should be thoroughly roasted in the oven till dry, yellowish brown, and crisp; biscuits and rusks should be treated in a similar way. Starchy foods are not well borne in this disease, the smallest quantity introduced too soon often causing relapse. If during convalescence or at any future time the tongue become sore, or dyspeptic symptoms reappear, or diarrhœa occur, it is advisable to administer some mild aperient as castor-oil or Gregory's powder, on the first indication of anything going wrong. Pending their action, the patient should starve. A pure milk diet must again be had recourse to for two or three days, before gradually returning to the usual food.

Sometimes the milk treatment fails. In these cases peptonising the milk may be tried; or a diet of meat juice, or one of underdone or scraped meat had recourse to. After a time on such a diet, it may be found that milk will now agree. If this on trial should prove to be the case, milk may be added permanently to the dietary.

Different medicinal remedies have been used for this disease; apparently little reliance can be placed on their doing any permanent good. A mild purgative at the outset, and at intervals, is advisable. Opium may be given with care if the diarrhœa is violent at any time; it may be combined with chalk or bismuth. Astringents are not advisable. At times peptonising substances may be added to the food with advantage; but, on the whole,

the treatment must be principally a dietetic and hygienic one. When sprue occurs in the tropics, or even when it is threatened, and does not at once yield to treatment, the patient should, if possible, return to Europe. During the winter and spring months, residence in the south of Europe or in some mild climate is advisable.

PATRICK MANSON.

DENGUE.

An infectious, epidemic, febrile disease confined to warm climates and characterised by a definite course, an initial and terminal exanthem, severe pains in the joints and muscles, and an insignificant mortality.

History and geographical distribution.—The earlist accounts of this disease date from 1779, and refer to epidemics in Cairo and in Batavia. Since that date many epidemics have been recorded as spreading along the trade routes all over the tropical and sub-tropical world. In Europe epidemics have occurred in Spain, Italy, and Greece. In 1889, dengue appeared in Syria, Asia Minor, Greece, and the neighbouring islands. The northern limit of dengue in the eastern world is 41' N., in the western 39' N. South of the equator it probably does not extend beyond the tropics. Apparently dengue is endemic in certain countries—as Egypt, the Sandwich Islands, Tahiti, the east and west coast of tropical Africa, and especially in the West India Islands.

Etiology.—The specific germ is unknown; nevertheless, local epidemics having frequently been traced to imported cases, there can be little doubt about the infectious nature of this disease. As the incubation period is very short, sometimes not exceeding twenty-four hours, rarely more than two days, and as the disease is generally very mild, seldom confining the patient to the house for more than a few days, and sometimes not at all, and as the patient's body continues to emit the infection for a considerable time after recovery and while he is mingling with the general population, the rapid spread of dengue in a community—so remarkable a feature in this disease—receives a ready explanation. High atmospheric temperature is the most important meteorological condition demanded; consequently outside the tropics dengue occurs only during the summer; cold weather at once puts a stop to an epidemic. Dampness or dryness of the atmosphere, the character of the soil, and elevation—apart from their effect on temperature—have no influence. Ship epidemics often occur.

During visitations of this disease, two-thirds, or three-fourths, or even a larger proportion of the inhabitants of the affected district are attacked. Neither age, sex, race, nor occupation have any marked influence on susceptibility. Neither is one attack invariably protective against a second; as with influenza, certain individuals appear to have a special predisposition and liability to recurrence. The lower animals also are said to suffer from dengue.

Morbid anatomy and pathology.—In the few recorded fatal cases, serous effusions in joints, pericarditis, and softening of the myocardium have been noted. The spleen is not enlarged.

Symptoms.—As a rule, prodromata are absent, the disease usually commencing with remarkable suddenness, the patient being well one hour and acutely ill the next. Slight shivering is quickly followed by high

fever, severe frontal headache, racking pains in the joints and muscles, a general sub-erythematous flushing of the skin—the primary eruption, bloated face, red eyes, photophobia, quick pulse and rapid respiration. In a few hours the temperature may reach 104° or over. The pains, sometimes excruciating, which constitute so characteristic a feature of dengue, affect the joints both large and small. The knees are a common seat; both they and other joints may in a few instances be red and swollen. The muscles are also attacked, and so are the bones—hence the term "breakbone fever," one of the many names applied to dengue. These pains come and go, and are aggravated by movement. They may persist during and for a long time after convalescence.

After one, two, or three days, the initial fever subsides either by crisis of sweating, of diarrhœa, of epistaxis, or by gradual defervescence. The patient then, apart from the pains which in greater or lesser degree may persist, now reverts to a condition of comparative comfort. This apyretic period, of from one to three days' duration, is again followed by a further but much slighter and more evanescent rise of temperature of, perhaps, a few hours' duration only, and the appearance of the terminal exanthem. This eruption is usually of a morbilliform character, appearing successively on hands, arms, face, trunk, legs, and feet. Sometimes it tends to become confluent, at other times to be patchy and irregular. After a few days it fades in the order of its appearance; to be followed in a proportion of cases, eight or ten days later, by furfuraceous desquamation, occasionally accompanied by falling of the hair and troublesome itching or hyperæsthesia of palms and soles. Convalescence is seldom delayed beyond the week; but it may be further protracted by such complications as boils, neuralgia, orchitis, psychical disturbance, diarrhœa, and the peculiar pains alluded to. There is great variety in the severity of the cases. In some epidemics relapses are not uncommon.

Diagnosis and Prognosis.—The exanthem, and the absence of profuse sweating during the fever, together with the nature of the concurrent epidemic, suffice to differentiate dengue from acute rheumatism. Scarlet fever, besides being very rare in the tropics, differs from dengue in the duration of the fever, in the severity of the throat symptoms, in the character and period of the eruption, and in the nature of the subsequent desquamation. In measles the catarrhal symptoms are more marked, and there are no severe joint pains as in dengue. In influenza the pains are absent or less severe, and catarrhal symptoms are common, whilst eruption is rare. Although fever and suffering may be great, the mortality from dengue is almost nil.

Treatment.—Aperients are not to be recommended, as the movements consequent on attending to calls to stool aggravate the pains. Fever may be relieved by sponging, ice to the head, cooling drinks, and two or three doses of antipyrine or phenacetin—drugs which also mitigate the pains. Diet should be light and digestible. The patient should keep to bed till after the disappearance of the terminal eruption. During convalescence an iron and quinine tonic is advisable. If pains persist, massage, electricity, iodide of potassium, or sulphur baths, will be found of use. A change of air is always advisable after severe attacks.

<div align="right">PATRICK MANSON.</div>

YELLOW FEVER.

AN acute, communicable tropical disease, with a remarkably restricted geographical distribution. Clinically, it is characterised by fever having a definite course, albuminuria, icterus, and a liability to hæmorrhages —particularly from the stomach. Parenchymatous fatty degenerations of liver and kidneys, and fatty degeneration of the heart and capillaries, are found post-mortem. The cause is believed by some to be a special bacterium.

History and geographical distribution. — Yellow fever was first reported in 1635. Since that date many epidemics have occurred in the endemic area which, roughly speaking, may be said to embrace the West India Islands, the coasts and islands of the Caribbean Sea and Gulf of Mexico, the coasts of Brazil and of west tropical Africa. The disease has occasionally appeared in European ports—in England, France, Spain, and Italy, but, with the exception of certain epidemics in Spain and Portugal, it has never obtained a firm footing in Europe. In America, the epidemics outside the endemic area have been more frequent and more severe. Yellow fever has occurred along the North American seaboard, as far north as Halifax; along the Mississippi Valley as high as St. Louis; in South America as far south as Monte Video; and also on the West Coast on both sides of the Equator. An important fact regarding yellow fever is that it may occur on shipboard on the high seas; only, however, after communication with an infected port or with an infected vessel.

Etiology.—The organism of yellow fever is believed by some to be *B. icteroides*, recently discovered by Sanarelli; we do not as yet know with precision the medium in which the infection enters the human body. Apparently, the germ is not water-borne.

Unlike the exanthematous fevers, yellow fever is not directly communicable from sick to healthy. It spreads only by a process of place, or soil, or ship infection. The germ certainly passes a part of its existence outside the human body before entering it. The virus, which under certain conditions is very tenacious of life, can be carried by man either in his ships, in his clothes, or about his body. For its development it requires a high atmospheric temperature, being most active if the heat is combined with damp; hence the rainy season in the endemic area is the most favourable for epidemic outbursts. Copious and long-continued rain, however, sometimes stops, decided fall of temperature checks, whilst frost at once puts an end to an epidemic. The germ is not always killed outright by cold; it may remain dormant during a long winter, and, reviving on return of warm weather, again cause a recrudescence of a suspended epidemic.

Large and densely-populated seaports are the favourite haunt of yellow fever. It invades, first and principally, the low-lying slums along harbours and docks; and exhibits the same preference for particular districts and houses which is so marked a feature in bubonic plague. Small inland towns and villages are rarely attacked. Although such have been recorded (Cuzco, 1855–56), epidemics are very rare in towns high above the sea level. Inside the endemic area yellow fever is kept alive during the non-epidemic intervals by sporadic cases, which every now and again break into an epidemic. Outside the endemic area epidemics are always introduced from without, and can generally be traced to some individual

or ship coming from a place where the disease is raging. In from four to eight weeks after such an importation, a few scattered cases having occurred in the meantime, it bursts out in epidemic force, and continues for a period of weeks, or months, or even of years, varying in intensity from time to time in harmony with meteorological and other circumstances.

Liability to yellow fever is singularly influenced by race and by duration of residence in the endemic area. The negro is very little liable, and, when attacked, the disease in him is much milder, as a rule, than in the European; the latter is likewise much more susceptible. Mongolians and mulattos occupy an intermediate position in these respects. Liability to yellow fever diminishes in a most marked manner with length of residence in the endemic area; this acquired immunity is partially lost when the endemic area is quitted temporarily. One attack of yellow fever is almost absolutely protective against a second. Sex has no marked influence on susceptibility. Childhood and old age are rarely attacked—10 to 30 being the age of greatest liability. The strong are more liable to attack than the weak and anæmic.

Morbid anatomy and pathology. — Besides the icterus and other lesions already mentioned, the skin may be the seat of petechiæ, and the muscles of more extensive extravasations of blood. Punctate hæmorrhages occur in most serous and mucous membranes. All tissues and fluids have a marked yellow colour. The heart frequently, though not invariably, is pale, dilated, and degenerated. The blood is dark and fluid. The capillaries are the subject of a fatty degeneration; hence one cause at least for the hæmorrhagic tendency. Black, grumous, acid, altered blood may be present in large quantities in the stomach and intestine. There may be hyperæmic patches, or even erosions, in the intestinal mucosa. In the early stages of the disease the liver is hyperæmic; but if death occur later this organ is usually anæmic, pale, and small, the liver cells containing a phenomenal abundance of fat, besides granules of a yellow pigment. The spleen is not affected. The kidneys are hyperæmic, and show cloudy swelling, with fatty degeneration and desquamation of the renal epithelium. The specific bacterium, according to Sanarelli, is found more especially in the liver.

Symptoms.—Yellow fever, although sometimes preceded by a day or two of malaise, generally sets in suddenly, often during the night, with sharp rigor or with alternating heats and chills. Restlessness, prostration, violent frontal and orbital headache, and pains in the back, loins, and legs are particularly urgent. The thermometer rapidly mounts to 103° or 104°, or even higher. The pulse is at first full and bounding, and the respirations rapid and shallow. The skin may be perspiring, or it may be hot and dry; occasionally erythematous eruptions, urticaria, sudamina, or pustules are noticed. The face is red and swollen; the eyes, injected and watery, shun the light. The tongue, at first moist and swollen, quickly becomes small, dry, and brown; the fauces and gums are congested. Thirst is urgent; anorexia complete. The epigastrium is tender, and there may be vomiting. The urine is scanty, acid, and, from the first, may contain a trace of albumin. This, the "primary fever," continues in ordinary cases from three to five days, occasionally as long as seven. During this stage the patient may die of suddenly developed hyperpyrexia. As a rule, however, the fever abates, and the patient enters on what is known as "the period of calm," a stage of almost complete apyrexia and of comparative

comfort, but also one of considerable prostration, in which the pulse is generally abnormally slow. Albuminuria is now almost invariably present. This stage may last two or three days, when the patient passes either into rapid convalescence, or into the third stage.

If the latter be the case, there is a return of fever, usually of a remittent character, in which the temperature ranges somewhat lower than during the primary fever; occasionally the rise of temperature may amount to a degree or two only. Delirium, sometimes of a furious character, more often low and muttering, supervenes; or, the mind remaining clear, there may be a complete apathy and prostration. The prominent symptom is the intense collapse. The features become shrunken; the pulse slow, small, and flagging. Epigastric tenderness and burning return, and vomiting may once more set in. The vomited matters, at first watery, gradually from increasing admixture of blood become dark and grumous like coffee-grounds; this is the well-known and justly dreaded " black vomit," an almost fatal symptom. Diarrhœa of a similar character may also come on. Occasionally pure blood is passed in the stool or is vomited. There is now anuria and a state of profound algidity, as in cholera. Consciousness may be maintained to the end; generally the patient falls into a stupor and such symptoms as singultus, Cheyne-Stokes' respiration, fibrillar twitching of muscles, or convulsions. precede death. Recovery from this condition of collapse is a rare event; it does occur, however, at times, the patient breaking out into a profuse perspiration and slowly entering on a protracted convalescence.

During the third stage of yellow fever, hæmorrhage may take place, not only from stomach and bowel, but also from nose, mouth, ears, eyes, lungs, kidneys, and other organs. If pregnancy be present, miscarriage is almost invariable.

The yellowness of the skin, from which the disease receives its name, does not always show itself during life, particularly if death has occurred early; but even in these cases it is invariably developed after death. Although it usually commences to appear towards the end of the primary fever, it may not be present until later—during the period of calm, or in the stage of collapse. The scleræ, the skin of the face, neck, and upper part of the trunk gradually acquire a pale yellow tinge, which steadily deepens to a deep orange colour, or even to a dark mahogany-brown. Notwithstanding the colour of the skin, there may be no bile in the urine, and the fæces may be normally coloured; the icterus, therefore, which may continue to increase, even after death, is hæmatogenous. Sometimes the bodies of yellow fever patients, even at an early stage of the disease, emit a peculiar and characteristic fishy odour.

Complications of various kinds—such as parotitis, boils, diarrhœa, and so forth—may delay convalescence. Relapse may occur and prove extremely dangerous.

The severity of yellow fever varies within wide limits. Abortive attacks, in which there is only an evanescent fever unattended by icterus and terminating in a crisis of diaphoresis, are not uncommon. Sometimes patients continue at their work during one of these mild attacks. Such cases may suddenly develop black vomit, with symptoms of collapse, and die. On the other hand, cases may be fulminating in character from the outset, and rapidly terminate in death on the first or second day.

The mortality from yellow fever varies very much in different races, in different epidemics, in different periods and localities of the same epidemic,

and also according to degrees of acclimatisation. It ranges anywhere from 5 per cent. to 75 per cent. of those attacked.

Diagnosis.—Mild cases of yellow fever may be hard to recognise. It is not always easy to say whether a given case of fever with icterus is yellow fever, or whether it is severe bilious remittent, or malarial hæmo-globinuric fever. Considerations regarding the nature of the prevailing epidemic, and the result of a microscopical examination of the blood, particularly the latter, are the most trustworthy guides. The occurrence of a period of calm, with slowness of the pulse, followed by rapid rise of temperature, together with albuminuria, point to yellow fever; splenic tumour and hepatic engorgement, to malarial disease. Flushed, swollen face; congested, sunken eyes; severe headache, and photophobia, suggest yellow fever. In all cases of doubt the blood must be examined microscopically.

Prognosis.—Prognosis is always doubtful, even in apparently mild cases. It is better for women and children than for men; for the spare, the anæmic, and the temperate, than for the stout, robust, and intemperate; worst of all for the newcomer. Danger increases in proportion to the rise of body temperature. The disease is rarely fatal if the temperature does not exceed 103°·5; always fatal when it passes 106°. If the primary fever continue beyond the third or fourth day, it is a bad sign. A scanty secretion of urine and copious albuminuria are also bad. Severe vomiting, early appearance of icterus, black vomit, and severe nervous symptoms, are all of them of grave import.

Treatment.—Prophylaxis, whether on shore or on shipboard, should include careful sanitation and a quarantine based on a five days' incubation period. During cold weather, yellow fever need not be apprehended. On the appearance of the disease in a town, the most perfect sanitation and the most rigid isolation and disinfection must be enforced.

There is no specific for yellow fever. At the outset a full dose of castor-oil or of calomel should be given; subsequently, aperients may be used only with the greatest circumspection. Frequently repeated hot foot-baths with mustard, or hot baths, are much used during the early stages, and are said to be beneficial. Cold applications to the head, and cold sponging of the body, and, in suitable cases, the cold bath, are the best antipyretics. Restlessness and insomnia may be treated with antipyrine or phenacetin in moderate doses; morphine is dangerous. Dry-cupping relieves loin-ache; sinapisms lessen epigastric distress; ice and small doses of cocaine may mitigate vomiting. Some prescribe astringents, such as perchloride of iron, for hæmorrhages. During collapse, alcoholic stimu-lants are necessary. Sternberg claims brilliant results from the systematic use of the following mixture:—Bicarbonate of soda, 150 grs.; bichloride of mercury, ⅓ gr.; water, 1 pint. Dose, three tablespoonfuls, given cold, every hour.

The feeding during yellow fever must be carefully attended to. No food should be given during the primary fever; later, an ounce or two of iced milk, or chicken-broth, may be given every three or four hours, or at shorter intervals in smaller quantities. If this provoke vomiting, feeding by the mouth must be suspended and nutrient enemata administered instead. During convalescence the diet for some days must be restricted to fluid nourishment; subsequently, only the most simple and digestible solids are permissible. Indiscretion in the matter of food is prone to cause relapse—a most dangerous occurrence.

PATRICK MANSON.

BERIBERI.

A SPECIFIC endemo-epidemic, multiple peripheral neuritis, occurring especially in warm climates. It is distinguishable from other forms of polyneuritis by marked tendency to implication of the pneumogastric, phrenic, and vasomotor nerves, by liability to dropsy, and by the frequency of sudden death from dilatation of the heart.

History and geographical distribution.—Our modern knowledge of beriberi begins with the writings of Bontius, who practised in the Netherlands Indies about the middle of the seventeenth century. Malcolmson wrote an excellent clinical account of the disease, as it occurs in British India, in 1835. Its recent recognition as a form of peripheral neuritis we owe particularly to Scheube, Bälz, Pekelharing, Winkler, and others.

Beriberi occurs in many parts of the tropical and subtropical world. Frequently met with in the tropical and subtropical regions of Asia, Africa, and America, it seems to be especially common in Brazil, the Eastern Archipelago, and Japan. Recently it has been seen among Chinese and aborigines in Australia. Although occurring principally in low-lying, damp, coast and river lands, it is not unknown in inland districts. The recent epidemics of polyneuritis in the Richmond Asylum, Dublin, in France, and in at least two lunatic asylums in the United States of America, appear to be of this or of a closely allied nature. Unlike malaria, it is as common in towns as it is in the country; and, also unlike malaria, it frequently breaks out among the crews, especially native crews, of ships trading in the tropics. Among these crews it is occasionally seen in our large seaports.

Etiology.—There have been many speculations as to the nature and cause of beriberi. With English writers there was a tendency at one time to regard it as a manifestation of scorbutus, of malaria, of rheumatism, or of anæmia. Some have attributed it to the use of diseased rice, others to a diet deficient in nitrogen. On examination, however, none of these views hold. A study of the epidemics shows unmistakably that beriberi has all the attributes of a specific and germ-caused disease. Amongst other evidences which could be cited in support of this view there are the facts that it can be transported by human intercourse from one place to another, and that it can be acquired only in certain districts, often only in limited localities in these districts. Were it dependent on causes such as those first mentioned, this liability to transportation, and these geographical limitations, would not obtain. Direct contagion has not been established, but there are on record several well-authenticated instances of the introduction of beriberi into a virgin country, and the subsequent spread of the disease there.

Although the germ has not been discovered, notwithstanding numerous efforts made in this direction, we know something about the conditions in which it flourishes. The principal of these are warmth, overcrowding, a high degree of atmospheric moisture, and damp. In the tropics it prevails mostly during the rainy season ; outside the tropics it occurs during the summer and autumn.

As regards distribution in the endemic areas, it is found that the disease is limited to certain houses, often to certain parts of these houses, particularly, though not necessarily, the ground-floor. It is prone to appear in prisons, in barracks, in schools, in convents, in mining camps, in

coolie lines on plantations, and in other places where large numbers of individuals live crowded together in unhygienic conditions. In ships it is most liable to occur among the native crews, when bad weather, or cold weather, cause the men to huddle together for warmth in dark, damp, and ill-ventilated forecastles. Once introduced into a house, school, ship, etc., it tends to become endemic, recurring over and over again, and year after year, especially in hot weather, or in the presence of unusual overcrowding and defective hygiene.

It is difficult to say what, as regards the human body, is the exact location of the germ or how it operates. Like the germ of malaria, it can live and multiply outside the human body; but whether it does or does not enter the body is uncertain. Some think that it does enter the body; I myself favour the idea that, residing in the soil, it manufactures there a toxine which, on being inhaled or swallowed, produces the characteristic neuritis.

Attacks of beriberi are apt to be provoked, after longer or shorter residence in the endemic area, by chills, catarrhs, shocks, over-fatigue, dysentery, unphysiological dietary, hardships, surgical operations, and so forth.

It affects all conditions of life, rich and poor alike; if anything, it has a predilection for the robust and the new-comer. It tends to recur in the same individual; in Japan, cases have been noted which have recurred every summer during a long series of years. A certain degree of immunity by acclimatisation may be acquired. Apparently the Malay rarely contracts beriberi in his own home, but the Chinese immigrant is very subject to it in the Malay country; and, it is said, if a Malay, immune to beriberi in his native place, migrate to some other beriberic spot, he may there acquire the disease.

All ages, excepting the very youngest, are liable; it is most prevalent between 20 and 35. Children under 8 years of age, and probably the very aged, are rarely affected. Although women are not so frequently attacked as men, pregnant and puerperal women are particularly subject to beriberi. Infants suckled by beriberic mothers acquire the disease.

Morbid anatomy and pathology. — The essential lesions in beriberi are those of a peripheral neuritis, with secondary degeneration and atrophy of the implicated nerves and muscles. The most important lesion, as affecting life, is that involving the pneumogastric nerve and its cardiac branches. To this are attributable the various cardiac symptoms, including the too often fatal dilatation of the right side of the heart. The œdema of the connective tissue, the occasional œdema of the lungs, and the serous effusions into pleuræ and pericardium, probably depend on similar implication of the vasomotor system. The central nervous system is not involved.

Symptoms. — Sometimes a trifling and barely noticeable affection, beriberi, on the other hand, is not unfrequently a disease of the utmost gravity. Between these extremes there is infinite gradation.

Prodromata in the shape of languor, pains, and weakness in the legs, transient numbness over the tibiæ, palpitations, cramp, and fever are occasionally, but by no means invariably present. Catarrhal symptoms and diarrhœa are sometimes noted. With or without these, rapidly or more slowly, the characteristic symptoms are evolved. For convenience, the various clinical types may be classified as—(1) Larval, (2) atrophic, (3) hydropic, (4) mixed, and (5) malignant.

Larval beriberi.—Patients complain of feelings of weakness or pains in the legs, numbness of the skin of the pretibial area and occasionally of the finger-tips, possibly of palpitation and of a certain amount of breathlessness; but they are able to be about, can walk with more or less difficulty, and in other respects feel and look well. On examining the legs, a certain amount of dulling of common sensation over the tibiæ, dorsa of the feet, perhaps of the thighs, fingers, and forearms, can be made out. Firm pressure against the bone shows that the calf muscles are distinctly hypersensitive. Knee-jerks after a time are usually in abeyance. Slight œdema over the tibiæ and ankles can generally be detected. Irritability of the heart, and perhaps a cardiac (usually systolic) bruit, coming and going, are generally to be made out. The case may linger on in this condition for weeks or months, a little better one day, a little worse the next, until finally symptoms disappear, or, on the other hand, slowly or more rapidly develop into graver forms of the disease.

Atrophic beriberi. — In this the muscles, particularly and invariably the muscles of the legs, and often of the thighs, hands, and forearms, and, in rare cases, of the trunk, rapidly undergo marked wasting. When the disease is fully developed, and is present in a high degree, the patient appears like a skeleton covered with skin. There is generally some œdema at an early stage, but this is always inconsiderable, and may disappear. Compression of the affected muscles causes considerable, often exquisite suffering; the knee-jerk and other deep reflexes, and, in extreme cases, the superficial reflexes, are abolished. Sensation in the skin over the atrophied muscles is diminished—sometimes, especially over the shins, almost abolished. The power of movement is impaired in proportion to the degree of muscular atrophy, and a certain amount of ataxia, in addition to mere muscular weakness, may be present. Walking may be impossible. The reaction of degeneration is invariably present in the affected muscles in all types of beriberi. Sometimes nearly all the voluntary muscles, with the exception of those of the face, eyes, and those subserving deglutition and respiration, are completely inoperative, and the patient lies on his bed absolutely unable to move. In these cases the functions of organic life may not be seriously interfered with; there is no fever, and, unless the muscles are roughly handled, little pain, although cramps and various paræsthesiæ may occur from time to time. In all the markedly atrophic cases there is evidence in palpitation, breathlessness, cardiac bruits, and often in increased præcordial dulness, in pulsating cervical vessels and epigastrium, of implication of the cardiac branches of the vagus and consequent dilatation of the heart. Sometimes the phrenic is also involved, and then there may be paresis of the diaphragm. Similarly, implication of the recurrent laryngeal nerve may give rise to aphonia from laryngeal paresis. The intercostal and abdominal muscles may also be affected. The sphincters are never attacked, and there is no tendency to bed-sores or other trophic affections of the integument

In all degrees of atrophic beriberi, and at any time in its course, the patient may die suddenly from syncope, or more frequently from a rapidly-developed dilatation of the right heart. In favourable cases—fortunately the majority—sensation and muscular power, after weeks or months, gradually return, and the muscles are entirely or partially slowly rehabilitated. Occasionally some deformity, as talipes equinus, may result from permanent atrophy or from permanent shortening of muscles.

Hydropic beriberi.—Like the atrophic form, hydropic beriberi, with

or without prodromata, may set in slowly or suddenly, be attended with urgent symptoms depending on cardiac or respiratory implication, or it may run a mild course without these fully developing. There is extensive general dropsy, with partial, sometimes almost complete, suppression of urine. Palpitation of the heart and cardiac oppression are usually prominent symptoms. Anæsthesia and muscular paresis of the legs or of the hands and arms may not be present; they are rarely so marked as in the atrophic type. There is a great tendency to serous effusion, especially into the pleuræ and pericardium, to the development of dilatation of the heart, to cardiac bruits, and to œdema of the lungs. After a variable time of weeks or months, profuse diuresis may set in; the bloated body then rapidly diminishes in bulk, the wasting of the limbs from atrophy of the muscles, if such has occurred, becoming now very apparent.

Mixed beriberi.—Atrophic beriberi may assume hydropic, and hydropic beriberi may assume atrophic, characters. Some cases from the outset are of a mixed nature, a fair amount of general or more local œdema concurring with well-marked muscular paresis.

Malignant beriberi.—A case from the outset may exhibit indications of grave cardiac and respiratory implication, palpitations and breathlessness constituting the most urgent symptoms; or such may supervene in the course of the ordinary atrophic, hydropic, or mixed types, particularly in the case of the two latter. In these very dangerous cases, attacks of breathlessness, palpitations, feelings of substernal and epigastric distress—often of a most acute and painful character—and restlessness recur at varying intervals. There is marked tendency to dilatation of the right heart as well as to pericardial and pleural effusion, sometimes to œdema of the lungs. At any time exacerbation of these conditions may set in, and the patient be suddenly seized with extreme dyspnœa, which very likely proves fatal in a short time, sometimes in a few minutes even. In bad epidemics such cases are common. Death has been known to occur within a few hours of the commencement of the disease.

Diagnosis.—Epidemic peripheral neuritis in warm climates is almost invariably beriberi. Pretibial œdema; muscular atrophy; tenderness of the muscles; palpitation and cardiac bruits; analgesia of the shins; absence (not invariable) of knee-jerks; non-implication of the ocular, facial, and pharyngeal muscles; absence of fever in the established disease, suffice, as a rule, to guide to a correct diagnosis. A not infrequent cause of confusion is the occurrence of peripheral neuritis in the intemperate within the endemic beriberi area; in such a case the history will be of great service. A very little attention to the symptoms and history will prevent confusion with such diseases as locomotor ataxia, progressive muscular atrophy, heart disease, nephritis, trichinosis, etc.

Prognosis.—The mortality of beriberi ranges in different epidemics from 2½ per cent. to 50 or even 70 per cent. of those attacked, varying very much according to the type of epidemic and the treatment adopted. Hydropic cases with great diminution of urine are, as a rule, more serious than atrophic cases, those with palpitation and other urgent signs of pneumogastric implication than the simple atrophic cases. Vomiting is always a grave symptom, indicating as it does advancing implication of the pneumogastric nerves. Signs of cardiac dilatation—as loud bruits, enlarged præcordial dulness, throbbing in the epigastrium and neck—are ominous. It is very unsafe to venture on a prognosis in beriberi, for, even in apparently mild cases, sudden implication of the pneumogastric may lead to a

rapidly fatal issue. The danger is especially great when the patient is obliged to remain on the spot in which the disease was contracted. On the whole, although, as stated, epidemics differ in fatality, beriberi is a more serious disease in the tropics than in higher latitudes.

Treatment.—The patient must at once be removed from the endemic area. His food should be light and nutritious; fresh vegetables, milk, eggs, fish, and meat being substituted for the rice on which he has probably been mainly subsisting. Experience has shown that bulky food, such as rice, is injurious in beriberi. If seriously ill, the patient ought to be kept in bed; if not very ill, he ought to spend most of his time in the open air. Sleeping-quarters should be well off the ground, dry, light, and airy. A saline aperient should be administered frequently during the more active stages of the disease; if the heart is feeble, irritable, and dilated, digitalis should be given regularly. During a paroxysm of dyspnœa, nitrite of amyl or nitroglycerin must be freely exhibited in full and frequently-repeated doses. There must be no delay in administering this remedy; nurses should be instructed in its use and informed of the indications for its prompt employment. If it fail to give immediate relief, the patient must be bled from the arm or external jugular; 10 oz. of blood will probably suffice, but the bleeding may have to be repeated subsequently. The over-distended right heart must be relieved at all risks. When the muscles are no longer tender, faradisation, massage, strychnine, and general tonics with change of air, especially a sea voyage, are of great service.

Disinfection, prevention of overcrowding, scrupulous cleanliness and dryness, sleeping off the ground in well-ventilated rooms, and, when feasible, the temporary abandonment of the affected quarters, are indicated in the presence of an epidemic. The food should be good and sufficient, and the clothing warm.

<div style="text-align:right">PATRICK MANSON.</div>

YAWS.

Syn., Frambœsia.

A CONTAGIOUS disease of the tropics, characterised by a short but somewhat indefinite incubation period; a prodromal fever, accompanied by rheumatic-like pains; and a fungating, encrusting, granulomatous skin eruption. It runs a chronic course of several months' or years' duration, and, to a certain extent, is amenable to mercury and the iodides. One attack is, as a rule, protective against a recurrence.

History and geographical distribution.—There has been some controversy as to the possible identity of this disease with the "sibbens" of Scotland and the "button scurvy" of Ireland. Probably they were not the same. At the present day yaws is found only within the tropics, and not everywhere there. It is particularly prevalent in the West Indies among the negroes, in tropical Africa, in Ceylon ("parangi"), in Fiji ("coko"), and the islands of the South Pacific; in Java, Burma, Assam, and probably elsewhere. In many of these places every child passes through an attack; in Fiji it is systematically inoculated (Daniels).

Etiology.—Although the germ has as yet not been recognised, there can be no doubt that yaws is a germ disease. Micro-organisms—cocci—

have been found in the lesions, but proof is wanting that these constitute the specific germ. Under ordinary circumstances, the disease is acquired by direct contact with a yaws sore, or the virus is accidentally applied by fingers, insects, dirty clothes, or otherwise. A breach of surface is necessary for infection. All races and all ages are susceptible, but, as can readily be understood, the disease occurs most frequently in the poor, the dirty, and especially in children, whose bodies are so often in warm climates naked and unprotected, and who do not appreciate the risks of contagion.

Morbid anatomy and pathology.—The yaw granuloma consists of round or spindle-shaped cells in a delicate and scanty stroma of connective tissue. It springs from the papillæ, which are much enlarged, and from the Malpighian layer.

Symptoms.—Ten to fourteen days after infection, and after a week or thereabouts of more or less fever, languor, rheumatic pain—often very severe, and, coincident with the decline of these symptoms, an eruption appears in the skin. The surface becomes dry and harsh, with here and there small circular patches of furfuraceous desquamation. These patches may be few in number and small, or they may be more numerous, larger, and tending to coalesce. After a further interval of a few days, minute papules appear in the scurfy patches, their eruption often being accompanied by much itching. Increasing in size, the papules burst through the epidermis, appearing like minute, red, hemispherical swellings, having at their apex a speck of a sulphur-yellow viscid material. This yellow material gradually extends over the whole of the little swelling, and, becoming dry and darker in colour, comes to form a complete crust. The papule may now shrivel up and disappear, leaving behind it a small pigmented spot. On the other hand, it may, and often does, continue to enlarge, forming a prominent excrescence varying in size from a pea to a walnut, or even larger. No matter what the size of the individual yaw, it is always, unless injured, covered by the yellowish or brownish crust, which tends to still further darken with age. If the crust is removed, the yaw, as these sores are called, is seen to consist of a red, smooth, rather soft, slightly bleeding, insensitive mass, exuding a yellowish gummy material, which speedily dries and becomes converted into a fresh crust. These encrusted excrescences sometimes attain a considerable size, perhaps in a few instances as much as an inch to an inch and a half in diameter and about three-quarters of an inch in height. When large they are flat on the top, and have somewhat rounded, everted edges; when small they are roughly hemispherical. Sometimes the yaw forms a ring surrounding a patch of healthy skin. Occasionally several yaws coalesce, particularly around the mouth, the nostrils, or on the nates. In these latter situations the surface, being prone to excoriation, is often raw and imperfectly encrusted. When yaws form on the sole of the foot, owing to the difficulty they have in breaking through the thick epidermis, they spread out laterally, attain a large size, and cause much pain, until the skin has been broken through and the granuloma has erupted.

In ordinary circumstances the individual yaw lasts for six weeks or thereabouts; it then shrivels up, the crust falls off, and a small pigmented scar remains. Occasionally a yaw breaks down and ulcerates.

The number of yaws varies from one to hundreds. The disease may cease on the healing of the first crop; usually, however, fresh eruptions occur from time to time, each relapse being preceded by a return of the

fever and rheumatic pains already referred to. In time the eruptions become more sparse, and gradually cease to recur.

An ulceration of the soft palate and nose has been described as a sequel of this disease. Some contend that this ulceration is of syphilitic origin, but as it is met with in Fiji, where, according to Daniels, syphilis is unknown among the natives, this cannot be the case.

Yaws is never congenital; it is not transmitted from mother to infant, or from infant to mother, unless by direct inoculation of the specific yaws' discharge into a breach of surface.

Diagnosis.—The presence of a lesion, such as described, following fever and severe rheumatic-like pains, and occurring in the endemic area, is diagnostic. There should be no difficulty in distinguishing yaws from any of the polymorphic lesions of syphilis. For many reasons, including absence of polymorphism, yaws is manifestly not a form of syphilitic disease, as some hold. In yaws there is no primary sore, no visceral disease, no gumma, no nerve lesions, no alopecia, no secondary sore throat, no congenital lesions; there is only one lesion, the yaw.

Prognosis.—As affecting life, yaws is not a serious disease. In the cachectic, however, the phagedenic type of ulceration, so common in the tropics, may attack the sores and prove dangerous. According to Daniels, the average duration of the disease is about one year; some cases may terminate in two or three months, whilst others may go on for as many years.

Treatment.—During the febrile rheumatic stage, everything should be done to encourage free eruption; warm baths, warm clothing, diaphoretics such as guaiacum, acetate of ammonia, and warm drinks are useful. Occasional aperients in moderation, of which sulphur electuary is a favourite, are also of use. When the yaws appear, some antiseptic ointment may be laid on the sores. The food ought to be good and plentiful; tonics may be administered from time to time. Iodide of potassium and mercury tend to cause involution of the tumours, but they do not, apparently, materially shorten the duration of the disease or prevent relapse.

Isolation of the sick, the protection of the body by clothes, the covering up of open sores, the destruction of soiled clothing, and such obvious measures for preventing contagion, should be enforced.

<div style="text-align: right">PATRICK MANSON.</div>

VERRUGA.

IN some of the lofty valleys of the Andes in Bolivia and Peru, a disease resembling, if not identical with, yaws, and locally known as "verrugas," is to be found. The same fever, the same rheumatic-like pains, and similar granulomatous excrescences on the skin, are present as in yaws; but in a large number of instances in verruga the fever and the rheumatic pains are much more severe and prolonged, and the skin lesion exhibits a remarkable tendency to bleed not seen in ordinary yaws. Oftentimes the hæmorrhage is so frequent and so profuse that a profound anæmia results, and death is by no means uncommon. The higher the altitude the more severe the disease, and the greater the liability to hæmorrhage. This is

well understood in the endemic districts; so that patients, where possible, descend to the sea-coast in order to diminish the risk. It is said that verruga is contracted only in certain limited districts. One place in particular, called Agua de Verrugas, has a very evil reputation in this respect; simply passing through this district, it is stated, may be enough to confer the disease, which here is said to attack domestic animals as well as man.

<div align="right">PATRICK MANSON.</div>

MALARIA AND MALARIAL DISEASE.

THE term malaria is virtually synonymous with *Plasmodium malariæ*[1]— a protozoon of warm climates, parasitic in man and in certain species of mosquito. In man it inhabits the red blood corpuscles, and gives rise to a special type of disease—malarial disease. Malarial disease is characterised by fever usually of a periodic character, anæmia, enlargement of the spleen, and the deposit in the tissues of a black pigment—melanin. Within the human body, the parasite, and consequently the disease it gives rise to, are, to a certain extent, amenable to quinine.

History.—Early in the history of medicine (Hipppocrates, 460–377 B.C.) fevers were already divided into continued and intermittent, that is malarial fever. Later, in the first century of the Christian era, clinical observation had arrived at distinguishing tertian from quartan intermittents (Celsus). Modern advance in the knowledge of malarial disease may be said to date from the introduction in 1640 of cinchona into Europe from South America by Cinchon, Viceroy of Peru; this drug supplied a valuable therapeutical test by which malarial fevers could be distinguished from non-malarial fevers with greater certainty than by their clinical features alone. Subsequent important steps in the history of the subject were the recognition of the malarial nature of certain pernicious fevers by Torti, 1712; Lancisi's investigations in etiology, 1716; the recognition of splenic enlargement as an important feature in the pathology of paludism, by Anduard, 1803 to 1823; the discovery of melanæmia by Meckel, 1847; and, most important advances of all, the discovery of the malarial parasite by Laveran, 1880, and of the rôle of the mosquito as its definitive host, by Ross, 1898.

Etiology.—The etiology of malaria may be conveniently treated under three heads:—(1) The parasite. (2) The physical conditions favouring the multiplication and diffusion of this parasite in external nature. (3) The conditions favouring (*a*) its introduction into, and (*b*) its multiplication in man.

The parasite.—This protozoal organism belongs to the Sporozoa, order Hæmamœbidia. In habit and structure it is closely allied to the Coccidia; like these it is an intracellular parasite, its particular cellular habitat in man being the red blood corpuscles. Many of the lower animals, particularly birds and reptiles, have similar, though not identical, intracorpuscular hæmoparasites. So far as is certainly known, the *Plasmodium malariæ* is peculiar to man. Seeing, however, that the plasmodium, as seems to be indicated by circumstantial evidence, may have an existence

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[1] Zoologically the malaria parasite is not a plasmodium. The only justification for continuing the use of the term is that it is now almost universally applied to this organism.

independently of man, it is more than probable that it has an additional host or hosts in outer nature belonging also to the animal kingdom; indeed, the same, or a closely allied, organism has been found in bats by Dionisi, and in monkeys by Koch. In the blood corpuscles of man the plasmodium exhibits two distinct phases, one (*a*) manifestly adapted for the multiplication and continuation of the organism in man; the other (*b*) in preparation for that phase of its life which is passed outside the human body. For convenience these two phases may be designated respectively *intracorporeal* and *extracorporeal*.

Intracorporeal phase.—There are several varieties, or it may be species, of plasmodia, each with a life-cycle of more or less definite duration —either of twenty-four (a rare form), of forty-eight, or of seventy-two hours' approximate duration. These varieties or species, although differing in minor morphological detail as well as in the duration of their respective life-cycles, are all of them, so to speak, constructed and developed on the same biological lines.

Though for a brief space during its earliest stage as spore, the plasmodium—then a minute, colourless, transparent sphere (Fig. 38, *f*)—is free in the blood plasma, it quickly enters on intracellular life by first attaching itself to and then penetrating a red blood corpuscle (Fig. 38, *a*). The young parasite, by assimilating the hæmoglobin in which it is now

a.   b.   c.   d.   e.   f.
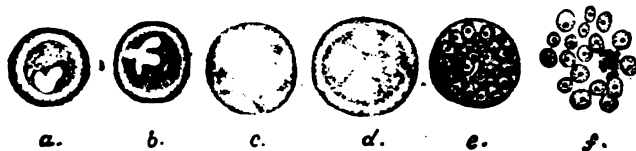
Fig. 38.—Parasite of tertian malaria.

embedded, increases rapidly in size, exhibiting at the same time active amoeboid movement (Fig. 38, *b*). Presently, grains—sometimes little rods—of an intensely black or very dark red pigment (melanin) appear in increasing numbers in the colourless hyaline substance constituting the growing parasite (Fig. 38, *c*). These pigment particles exhibit slow translation movements of their own, as well as changes of position brought about by the amoeboid movements of the parasite. When the plasmodium has about attained its full size, which, according to species, may be quarter, or half, or even greater than that, of an ordinary blood corpuscle, the pigment can be seen scattered irregularly throughout its substance (Fig. 38, *d*); but when the parasite is quite full grown, the amoeboid movements cease, and the pigment grains become concentrated into one or two clumps located usually about the centre of the little organism (Fig. 38, *e*). The protoplasm forming the mass of the animal now divides into spherules, which vary in number and size according to species; these are the spores. The pigment, being excrementitious or residual matter, does not partake in this process of division, but remains isolated and passive. The mature, sporule-bearing plasmodium thus constituted is usually called a "rosette" body. On the completion of sporulation, the blood corpuscle in which the parasite had developed disintegrates, and the contained plasmodium becomes free in the blood (Fig. 38, *f*). The spores then fall apart; such of them as escape the phagocytes enter fresh blood corpuscles and repeat the cycle. The pigment and many of the spores are taken up by the phagocytes.

It is to be noted that the plasmodia tend to occur in the blood in crops or swarms, all the parasites composing a particular swarm being about the same age, size, and stage of development. The parasites of each swarm, therefore, mature and sporulate, approximately, simultaneously, the successive generations maturing about the same hour daily, or every second or every third day, according to species. Two or three swarms of different ages may be present at the same time; so that double infection by a forty-eight hour parasite will have one swarm maturing to-day, another to-morrow. A treble infection with a seventy-two hour parasite will show a similar quotidian sporulation.

By staining the parasite with methylene-blue or other suitable pigment, its minute structure is revealed (Fig. 39). From the spore to the adult stage it is unicellular (Fig. 39, *a–d*). The cell consists of (1) a nucleolus rich in chromatin and eccentrically placed in (2) a vesicular, unstaining nucleus; and (3) an outer zone of colourable protoplasm in which the melanin particles are located. For a short time before sporulation, nucleus and nucleolus are not discoverable, having, by karyokinetic division (?) or otherwise, become fragmented and diffused through the mass of the parasite (Fig. 39, *e*); subsequently they reappear as the nuclei and nucleoli of the spores (Fig. 39, *f*).

Extracorporeal phase.—After blood from the subjects of malarial infec-

a.   *b.*   *c.*   *d.*   *e.*   *f.*
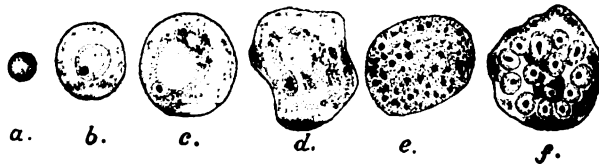
Fig. 39.—Evolution of the benign tertian parasite.—Compiled
from Mannaberg.

tion has been on the microscope slide for some time, in addition to the foregoing forms a peculiar multiflagellated organism (Fig. 40, *c*; Fig. 41, *e*), displaying great activity, is sometimes encountered. From the characters of the bioplasm of which it is principally composed, and of the melanin particles it contains, as well as from other considerations, it is evident that this singular body is a phase of the plasmodium. If we examine malarial blood often enough and at suitable times, sooner or later we will encounter the flagellated body in process of development, and learn that it is evolved from certain free spherical plasmodia (Fig. 40, *b*; Fig. 41, *c, d*). We may further learn that these free spherical plasmodia originate in one of two ways, according to the species or variety of plasmodium to which they belong. In what are known as the quartan and benign tertian parasites, the flagellated body originates from a sphere which originally resembled an ordinary full-grown intracorpuscular plasmodium (Fig. 40, *a*); in what may be designated the malignant parasites it originates from a peculiar form of the plasmodium called the "crescent body" (Fig. 41, *a*).

In the case of the quartan and benign tertian parasites, a full-grown plasmodium (Fig. 40, *a*) may sometimes be seen to escape from a red blood corpuscle—the corpuscle in which it had developed—and assume a spherical form (Fig. 40, *b*). By and by the pigment it contains becomes agitated, as it were, being driven hither and thither by some unseen force, the entire parasite the while rapidly changing shape and becoming violently jerked

about.   Presently one or more long flagella are suddenly projected from its periphery (Fig. 40, *c*), and immediately commence to wave about in a characteristic manner.

In the case of the malignant tertian and, possibly, other varieties of what are known as æstivo-autumnal plasmodia, the sphere from which the flagellated body is evolved is derived, as stated, from the crescent body (Fig. 41, *a*).   This body is also intracorpuscular; but, unlike the other intracorpuscular forms, it does not show itself in the blood at the commencement of the active manifestations of malarial infection.   It does not appear until about a week or ten days after the commencement of acute symptoms.   On their first appearance the number of crescents is small, but, as time goes on, they gradually become more numerous;
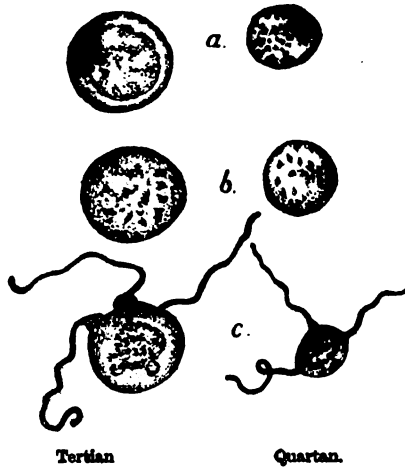
Tertian   Quartan.

Fig. 40.—Evolution of the flagellated body in the tertian and quartan parasites.—Compiled from Thayer and Hewetson.

then, after a week or longer, unless there is recurrence of fever, they gradually begin to disappear again.   This "crescent body" is, as its name implies, shaped like a crescent, with the exception that the horns of the crescent are more or less rounded.   It is colourless and somewhat glistening.   At or near its centre a cluster of melanin granules is always a prominent feature.   By careful scrutiny, especially if aided by staining, we can make out that it is enclosed in the almost colourless remains of a red blood corpuscle, part of which can be seen as a delicate bow uniting the horns and bridging across the concavity of the crescent.

Fig. 41.—Malaria parasite: evolution of the flagellated body from the crescent.

The earlier stages of the crescent body are not readily recognisable in the peripheral blood, if indeed they occur there; most probably the crescent is wholly evolved in the vessels of some of the viscera—spleen, bone marrow escaping into the general circulation when approaching maturity.   I am inclined to agree with Mannaberg in regarding the crescent as what in zoological language is called a *syzygium*, that is an organism resulting from the conjugation of two individual organisms, in this case two ordinary plasmodia in a multiple infection of a blood corpuscle—no unusual occurrence.   I likewise believe that the spheres from which the flagellated bodies of tertian and quartan infections are evolved also originate in a double infection of a corpuscle.   This conjugation of two parasites I regard as the circumstance determining the peculiar direction taken by development in those of the plasmodia that are destined for extracorporeal life.

If in a suitably prepared slide the crescent body be watched, it can be seen in the majority·of instances to slowly change shape, becoming oval (Fig. 41, *b*), then spherical (Fig. 41, *c*), the remains of the blood corpuscle at the same time falling away and leaving the parasite naked in the blood. In a variable time, usually from fifteen or twenty minutes after the blood has been mounted, the pigment, which has now arranged itself as a distinct ring at the centre of the sphere, in many of the spheres begins to move. These movements, at first slow, become progressively more violent, being apparently directed to breaking through a delicate and invisible capsule, which at this stage may enclose the central portion of the spherical body. At first this hypothetical capsule resists the efforts which the pigment appears to be making; presently, however, it seems to rupture, and the pigment it hitherto confined becomes diffused throughout the entire sphere (Fig. 41, *d*). Simultaneously with this the central and pigment-bearing part of the parasite becomes jerked about, repeatedly and rapidly changing shape. Careful observation, aided by staining, shows that these movements are produced by flagella which, attached to the central pigmented portion of the sphere, are waving about very actively. Finally these flagella, bursting through the delicate peripheral capsule of the sphere, are thrown out from one, two, or more points in the periphery of the little body (Fig. 41, *e*). Sometimes the flagella are isolated, sometimes they are in more or less tangled bundles. It is probably in consequence of the efforts of the flagella to erupt that the jerking, agitated movements of the sphere are produced.

In both types of flagellated body the flagella may vary in number from one to six, or even more. They are very slender and of great length— three to five times that of the breadth of a blood corpuscle. Here and there, either in their continuity or at their free extremities, they may be expanded into a sort of bulbous thickening (Fig. 41, *e*). For a time the flagella remain attached by one end to the parent body, vigorously waving about, and lashing and bending the blood corpuscles. While thus attached, they resemble so many wriggling eels held fast by their tails. After a time, many or all of the flagella break away and swim free and independently in the liquor sanguinis. They continue to move in this way for a considerable time—two hours in some instances, and have even been seen to attack leucocytes (Ross). Those flagella which do not succeed in breaking away from the parent body, gradually slow down in their movements, some of them vanishing as if by slow solution; others, before vanishing from view, coiling themselves up like the tendrils of a vine.

The residual body remaining after the eruption of the flagella consists of a small portion of protoplasm which now contains all the melanin. Its movements quickly cease; very generally it is engulfed by a phagocyte. Frequently non-flagellated spheres and the flagellated bodies themselves are attacked by the phagocytes, which, however, respect the crescent bodies, and, at all events in the peripheral circulation, all intracorpuscular plasmodia.

The spheres, whether crescent-derived or directly escaped from the blood corpuscles, are of two kinds—hyaline and granular; the hyaline alone gives rise to flagella, the granular never exflagellate.

At one time the flagellated forms were regarded by many observers as moribund organisms in their death agony, the whole series of remarkable phenomena exhibited by them being supposed to have no reference to the life history of the parasite. In 1894, and again in 1896, the writer, basing his

hypothesis on the regularity with which exflagellation occurs in all varieties
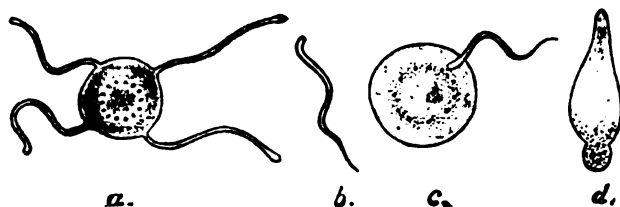
FIG. 42.—*a*, Microgametocyte emitting four microgametes (flagella);
b, free microgamete; *c*, fecundation of the macrogamete; *d*,
zygote (travelling vermiculi).

of the parasite, and on the suggestive fact that it occurs only when the
parasite is removed from the human body, published the view that the flagel-
lated body was no mori-
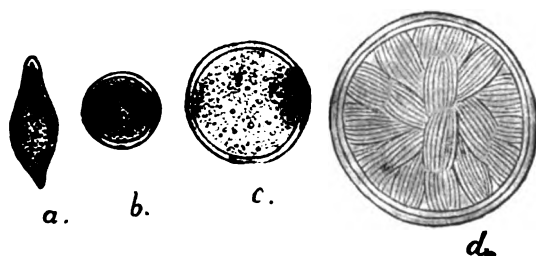
FIG. 43.—Transformation of the zygote in the stomach
wall of the mosquito.—After Grassi.

bund organism, but that it
had reference to the extra-
corporeal phase of the
parasite. Further, con-
sidering that there ap-
peared to be no provision
in the structures of the
parasite which would
enable it to escape spon-
taneously from the human
body, as there is no
evidence that it is ex-
truded from the human body in excretions or in morbid discharges,
and as the plasmodium, like all parasites, must contrive in some way to
keep in existence as a species by passing from
host to host, he inferred that some extraneous
agency must come into operation to remove it
from the human body. The plasmodium being a
blood parasite, this agency, he concluded, must be
a blood sucker; and from considerations based on
the distribution of malaria in nature, and guided
by the analogy of what occurs in the case of
Filaria nocturna in similar circumstances, he
further concluded that this blood sucker must be
the mosquito, and probably a particular species
of mosquito.

Working on the lines indicated by this hypo-
thesis, Ronald Ross has shown, and his observa-
tions have been abundantly confirmed as well as
extended by Grassi, Bignami, Celli, Koch, Daniels,
and others, that if certain species of mosquito
belonging to the genus *Anopheles* are fed on
malarial blood, spheres and flagellated organisms
rapidly form in the stomach of the insect, and,
passing into the wall of the stomach, undergo
a remarkable process of development eventuating in the formation of a
multitude of *sporozoites* which ultimately find their way into the cells and

FIG. 44.—Zygotes protruding
on the outer surface of the
mosquito.—After Ross.

secretions of the veneno-salivary gland, whence they are transferred to the blood of any human being the insect should chance to attack. Ross has found that an exactly corresponding evolution is gone through by the flagellated and spherical forms of *Proteosoma,* a malaria-like parasite of certain birds (sparrows, etc.), but that in this case the appropriate mosquito host belongs to the genus *Culex.*

Direct observation of the human parasites, supported and supplemented by the analogy of the corresponding parasites of birds (*Halteridium* and *Proteosoma*), indicates the following as the complete life history, intracorporeal and extracorporeal, of the malarial parasite:—In its earliest phase the parasite is an *amœbula* or *myxopod* (Fig. 38, *a*), which, entering a red blood corpuscle, grows, becomes pigmented, and develops into (*a*) a *sporocyte* (Fig. 38, *d*), or (*b*) into a *gametocyte* (Fig. 38, *f*).

(*a*) The *sporocyte* divides into a number of naked *spores* (Fig. 40 and Fig. 41, *a*), which, on being set free, enter fresh blood corpuscles, becoming amœbula once more, and so continuing the process in the human body, as already described.

Fig. 45.—*a*, Rupture of zygote cyst into the body cavity of the mosquito; *b*, free sporozoites.— After Grassi.

(*b*) The *gametocytes* (crescents, and the large intracorpuscular forms which do not sporulate) obtain their opportunity of developing by being ingested by the mosquito. They are of two kinds, *hyaline* (male) (Fig. 42, *a*) and *granular* (female) (Fig. 42, *c*). The hyaline emit a number of *microgametes* (the flagella), which, breaking away (Fig. 42, *b*, *c*), seek to enter the granular gametocyte (*macrogamete*). One microgamete succeeds in effecting an entrance. Thereupon the macrogamete as a result of this act of impregnation changes shape, becoming an elongated, spear-shaped *zygote* (Fig. 42, *d*), the pigment granules accumulating at its broader or posterior end, the anterior end becoming finely pointed (MacCallum). The zygote thus formed acquires powers of locomotion, penetrates the wall of the mosquito's stomach, and becomes lodged in the meshes of the muscular layer of that organ. There it assumes a spherical or oval shape, becomes encapsulated, and grows rapidly—from 6 μ to 70 μ—the nucleus and protoplasm dividing up into a number of *blastophores*. On the surface of the blastophores, slender, spindle-shaped *sporozoites* are now developed in vast numbers (Fig. 43). The blastophores next disappear, and the capsule, packed with sporozoites, protrudes like a wart on the external wall of the stomach (Fig. 44). The capsule then ruptures, and the sporozoites escape into the body cavity of the insect (Fig. 42, *a*, *b*), whence, as already stated, they find their way into the blood, and finally into the cells and ducts of the veneno-salivary gland, to be injected into the blood of any human being the infected mosquito may chance to attack. From a week to ten days after being bitten by an infected mosquito, the red blood corpuscles begin to exhibit parasites, and the clinical phenomena of malaria declare themselves.

There are undoubtedly several forms of plasmodium; but whether these are specifically distinct one from the other, or whether they are merely transmutable varieties, is still an open question. The bulk of opinion is in favour of regarding them—at all events certain of the forms

—as distinct species. The table on p. 298, modified from Mannaberg, gives the principal characteristics of the more important types.

The student, in order to acquire a working knowledge of the *P. malariæ*, must avail himself of every opportunity to study the various forms of the parasite he may find in malarial blood, comparing them with the plates, and with the descriptions of species in the following table. If he does so, he will with practice acquire a familiarity with its microscopical appearances of the utmost value in the diagnosis, prognosis, and treatment of malarial disease.

What are the evidences that the plasmodium is the cause of malaria? First, in every case of malarial disease which has not been treated by quinine, it is possible to find the plasmodium. Second, the plasmodium has been found in causal relationship to no other disease. Third, the cycle of the plasmodium, as will be described presently, is found to coincide with the cycle of the special form of fever it is associated with. Fourth, melanæmia and a special form of pigmentation of viscera have long been regarded as pathognomonic of malaria; the melanin, the source of this pathognomonic feature, is manifestly a product of the plasmodium. Fifth, quinine, which cures malarial fever, rapidly causes the disappearance of most forms of the parasite from the blood; not, however, the crescent-derived forms, which, as will be shown, are not fever forms. Sixth, experimental intravenous injection of malarial blood is followed by malarial fever and appearance of plasmodia in the subject of the experiment. Seventh, the bite of mosquitoes, whose salivary glands are known to contain the sporozoites of the malaria parasite, is followed by the appearance of the malaria parasite in the blood of the person bitten and by the clinical phenomena of malaria.

Physical conditions determining geographical distribution.—The distribution of malaria is regulated by the physical conditions demanded by the particular species of mosquito subserving the parasite.

As already stated, these mosquitoes belong to the genus *Anopheles*. Evidence is accumulating that several species of this genus are efficient hosts. In Italy, *A. claviger*, *A. pictus*, *A. bifurcatus*, and in India *A. rossii* have all been incriminated. Hitherto the malaria parasite of man has been found in no member of the genus *Culex*. The same remark applies to the various species of the other genus of European *Culicidæ*, namely, *Ædes*.

The species of these three genera of mosquito can readily be recognised by the length of the palpi in the sexes. In *Anopheles* the palpi are long in both sexes, equalling in length the proboscis; in *Culex* they are long in the male insect, but very short in the female; in *Ædes* they are short in both sexes. According to Ross, *Anopheles* when at rest poises approximately at right angles to the surface it is clinging to; whereas in similar circumstances the body of *Culex* is on a parallel plane. Further, the larvæ of *Anopheles* when breathing lie parallel to the surface of the water they live in; those of *Culex* hang head downwards at right angles to it. *Anopheles* requires puddles of water in which certain algæ are growing; *Culex* is not so fastidious, but breeds in almost any collection of water.

In atmospheric temperatures below 60° F., in dry sandy deserts, and on board ship at sea, malarial disease, although it may occur as a relapse, is never contracted for the first time. From this it may be inferred that *Anopheles* requires a combination of warmth, moisture, and certain as yet unknown telluric conditions.

Tabular Statement of the Characteristics of the Various Malarial Parasites.

	Duration of Cycle.	Movement.	Pigmentation.	Maximum Size.	Form of Spore Formation.	Number of Spores.	Crescentic Bodies.	Alterations in the Infected Blood Corpuscles.
I. Quartan parasite (Fig. 46).	Seventy-two hours.	Slight movement in the immature forms.	Coarse grains; little or no movement.	The size of the red blood corpuscles.	Daisy form; the single spores roughish, with distinct nucleolus.	6–12.	None.	The red blood corpuscles are little discoloured, and do not alter their size.
II. Benign tertian parasite (Figs. 38 and 39).	Forty-eight hours, or less in anticipating types.	Active amoeboid movement in the immature and also in the middle-aged forms.	Fine granules in immature forms; often in the larger, actively swarming.	Size of the red blood corpuscles, sometimes even larger.	Sunflower or grape-like; single spores small, round; nucleolus rarely seen.[1]	15–20 (oftenless).	None.	The red blood corpuscles are often hypertrophied, and lose colour quickly and often completely.
III. Pigmented quotidian parasite.	Twenty-four hours.	The unpigmented, immature form very actively amoeboid; less active when pigment accumulates.	Very fine; later coalesces in one or two lumps; does not swarm.	½–¾ the size of a red blood corpuscle.	Irregularly-formed heap.	6–8 (even more).	Present.	The red blood corpuscles shrink often, and are then either darker stained (copper colour), or may be completely decolorised.
IV. Unpigmented quotidian parasite.	Twenty-four hours or less.	Very active amoeboid movement.	None.	½–¾ the size of a red blood corpuscle.	Star-shaped, or in irregular heaps.	6–8.	Present.	The red blood corpuscles shrink frequently, and are dark in colour
V. Malignant tertian parasite (Figs. 41 and 47).	Forty-eight hours, or less in anticipating types.	Active; the movement remains present in the pigmented bodies.	Moderately fine; often shows oscillatory movement.	½–¾ the size of a red blood corpuscle.	Irregular heaps.	10–12 (rarely 15–16).	Present.	The red blood corpuscles shrink frequently; they are dark coloured, or may be perfectly colourless.

[1] N.B.—In the fresh condition; it is always seen in stained preparations.

From the fact that within the endemic belt malaria is prone to occur in low-lying lands, about the estuaries of great rivers, along the sea-board, in jungle lands, and in swamps, great significance has been attributed to the presence of decaying vegetation and of abundance of water as generators of the germ. But although the presence of decaying vegetation is a frequent concomitant, and, it may be, a favouring condition, neither this nor excessive moisture are essential; for malaria is common enough on many dry table-lands, on bare rocky places, and in barren spots in which water is scarce, and vegetation is of the most meagre description. Neither, on the other hand, does the combination of heat, moisture, and decaying vegetation always suffice for the generation of malaria. There are many places—certain of the South Pacific Islands, for example—in which these
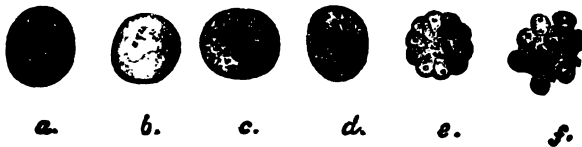
Fig. 46.—Parasite of quartan malaria.

conditions all coexist in a high degree, and yet malaria is unknown. Manifestly, the conditions required by *Anopheles* are of a very complex character.

Outside the human body, the plasmodium, regarded as simply an organism in nature, is but one among myriads of competing forms. The same remark applies to its extracorporeal host. That the plasmodium and its extracorporeal host shall survive in any particular locality demands, therefore, a number of conditions. First, the locality must afford the meteorological and telluric conditions already indicated as necessary; second, the plasmodium and its mosquito host must predominate over, or hold their own with, such competing forms of life as may happen to coexist in the locality ; third, their enemies must be few, relatively
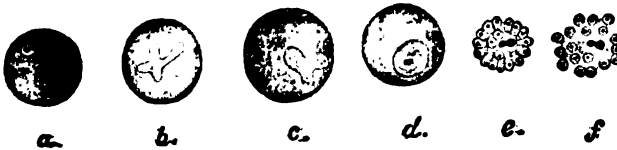
Fig. 47.—Parasite of malignant tertian (æstivo-autumnal) malaria.

feeble, or absent. The plasmodium is a part of nature, and, seeing that it has to live in external nature before it can find a safe asylum in man, is subject to the laws of survival affecting all organisms. These considerations—the presence of a suitable extracorporeal host, the absence of competing forms, and the absence of enemies—are generally lost sight of in discussing the etiology of malaria; nevertheless they are only second in importance as affecting the distribution and presence of malaria to temperature, moisture, and soil.

Most probably there are many places which owe their healthiness, not to the absence of telluric and meteorological conditions suitable to the extracorporeal phase of the plasmodium, but to the presence of some enemy of *Anopheles*, or some competing form which overpowers it, and so keeps it under. Studies on these lines have not been commenced.

Meanwhile certain facts about the distribution of malaria, which in the future will possibly receive their explanation by such studies, are known. Malaria, although it has occasionally been found almost as far north as the Arctic Circle, increases on the whole in frequency and intensity as the Equator is approached. It is not evenly distributed over this vast area; on the contrary, it occurs in what might be called scattered pockets. These pockets become more numerous and larger in area towards the Equator. They are often very limited in extent, being confined sometimes, it may be, to a few square yards. Thus one house may be malarious whilst the neighbouring house is healthy; one room even may be malarious whilst the other rooms in the same house are not so. One side of a valley may be healthy, the other unhealthy. One island may be healthy, a neighbouring island unhealthy. In our ignorance of the determining factors, we are apt to regard the distribution of the plasmodium as capricious. This caprice is apparent only; for did we know more of the life-history of the plasmodium outside the human body, more about its mosquito hosts, and more about the competing forms, this apparent caprice would receive a rational explanation. Temperature, moisture, and soil are important, but they are not the whole of the problem.

The difference in frequency of malaria in warm as compared to cooler countries is in great measure dependent on atmospheric temperature. This being so, altitude, inasmuch as it usually implies lower temperature, should also diminish malaria; and this is generally the case, for experience has shown that on the whole the hills are healthier than the plains. Exceptions to this rule are numerous enough, for altitude *per se* has no influence on malaria. If altitude means low temperature, then, as regards malaria, it makes for salubrity; but a valley which is badly drained, hot, and confined, even if at a considerable altitude, may, notwithstanding its elevation, be malarious.

The influence of water in furthering the development of malaria is generally recognised. Waterlogging of the soil by floods, or by the artificial raising of the level of the ground water through systems of artificial irrigation, canals, embankments and so forth, is dangerous. These things tend to make what was a dry, healthy country a damp and malarious one; doubtless by affording good breeding opportunities for the malarial mosquitoes. Possibly for the same reason, breaking up waste lands for cultivation; allowing ground to fall out of cultivation; earth-cutting for railways, roads, canals, foundations, and soil disturbances generally are prone to be followed by epidemics of malaria. Covering the soil as with houses, pavement, tillage, or deep-flooding with water, tends to suppress malaria.

Malaria, that is the extracorporeal host of the plasmodium, usually cannot survive transport for more than a few yards; nor can it rise more than a few feet above the spot in which it originated. At the same time, in certain unknown conditions, it may be introduced into and flourish in places previously free; as happened, for example, in 1867 at Mauritius and, later, at Réunion. Like the germ of smallpox or of measles, it does not retain its vitality for a long time, or for a considerable distance from its source, unless, whether intentionally or by accident, it be specially protected.

In tropical countries certain seasons and years are more malarious than others; but the unhealthy season is not the same for every country. In some it is the dry season, in others it is the rainy season. These

apparent discrepancies are explained by the influence on the breeding pools of *Anopheles.* In subtropical countries malarial fevers from first infections begin to show themselves in the early summer, and are most severe in late autumn; fevers from first infections do not occur during the winter and spring.

Circumstances favouring introduction and multiplication in man. —The most important of these is residence in a malarial locality. There can now no longer be any doubt that the malarial parasite is sometimes, if not always, injected into man by the mosquito during haustellation. There may be other ways by which it can be acquired, but as yet we have no experimental knowledge of such. Ross observed in mosquitoes fed on proteosoma-containing blood, and similar observations have been made on mosquitoes fed on malarial blood, that certain of the zygote capsules in the stomach wall of the insect contained large, black, sausage-shaped bodies. These, apparently, undergo no development in the mosquito in which they occur; but there is some reason for supposing that they represent another phase of the malarial parasite, one functioning as a resting spore, and intended for subsequent development either in man, some other vertebrate, or in succeeding generations of mosquitoes independently of a vertebrate intermediary. One can conceive that such bodies might lie latent in soil or water, and so in water or through the air get access to man, other vertebrates, or to the mosquito.

It is generally believed that malaria is most abroad just before sunrise and just after sunset; experience has shown that exposure in malarious spots at these times is apt to be followed by malarial infection. The fact that sleeping on the ground in malarious localities is also apt to be followed by infection, tends to show that the plasmodium is most abundant in the lowest stratum of the air. · These and other considerations have their explanation in the habits of the mosquito, the nocturnal habits of this insect, together with the fact that it clings to the neighbourhood of the ground; that the plasmodium, in fact, is a parasite of the mosquito as well as of man.

A lowered condition of vitality, such as may result from fatigue, cold, damp, exposure, depressing emotions, idleness, dissipation, apparently by depressing resistance favours the establishment and proliferation of the plasmodium once it has obtained a lodgment in the human body.

Age, sex, occupation.—Age has no very manifest influence upon susceptibility. Children are just as liable as adults; in the former malaria is, on the whole, a more common and serious disease than in the latter. Sex, as such, has no special influence; neither has occupation, though, of course, those engaged in working the soil are particularly liable to infection.

Infection.—Malaria is not directly communicable from one human being to another by any natural process of infection; but if blood from a malarial subject be injected into the circulation of a non-malarial, the latter, after an incubation period of from eight to twelve days, will very probably have an attack of malarial fever of the same type and associated with the same variety of plasmodium as in the former.

Immunity.—One attack of malaria, so far from producing immunity, is generally followed by subsequent attacks; and this whether the attacks be the result of relapse or of fresh infection. Observations by Koch, confirmed by Stephens and Christophers, have recently shown that in intensely malarial districts practically all the young children have malaria

parasites in their blood. As the native children get older, their blood is progressively less liable to the infection, and in native adults the parasite is rarely found. Immunity from malaria can therefore be acquired. Whether this fact can be turned to practical account has not been determined.

Morbid anatomy and pathology.—The post-mortem appearances in malarial fever are characteristic. The spleen is invariably enlarged, sometimes very much enlarged. In recent cases it is softened, almost diffluent. On section it is found to be dark brown in colour, what is called "pigmented." The liver is also enlarged, congested, pigmented, and softened. The vessels of the brain are full; the grey matter often of a dark, sometimes of a leaden hue. The marrow of the spongy bones is also dark and congested. Minor degrees of pigmentation and congestion are found in the lungs, alimentary canal, and kidneys.

On submitting the various organs mentioned to microscopical examination, plasmodia and their product melanin are found in great abundance within the blood vessels. In the spleen and bone marrow the parasites are specially abundant, and occur, both inside and outside the vessels, included in the large phagocytic cells proper to these organs. Some of the large splenic cells may contain not one but many parasites still enclosed in the blood corpuscles in which they had developed, also parasites apparently not so enclosed, and masses of pigment; they may also contain melaniferous leucocytes. As the spleen is not only the grave for defunct parasite-infested blood corpuscles, but also a principal breeding-ground for the plasmodium, the blood of the splenic vein is richer in parasites and melaniferous cells than that of any other vessel in the body. The vessels of the liver likewise contain many plasmodia and much pigment; pigment granules can readily be seen scattered in and along the vessels. The capillaries of the grey matter of the brain are sometimes so crowded with parasite-infested corpuscles that they are virtually thrombosed thereby. The intestinal mucosa, the epiploon, and the kidneys may be similarly affected, though to a slighter extent.

In addition to the melanin pigment which is so prominent a feature in the histology of malaria, and which, unless in the spleen and bone marrow, is confined to the vessels, there is to be found another pigment—a yellow pigment. This yellow pigment, unlike the melanin, is not confined to the blood vessels, but is deposited in the cells of the liver, spleen, kidneys,—in fact, in nearly every organ and tissue of the body. It occurs in the protoplasm of the cells as minute grains. Chemical tests prove it to be slightly altered hæmoglobin, derived, doubtless, from the blood and deposited in the protoplasm of the tissue cells; just as happens in many other diseases, in burns, and in forms of poisoning associated with rapid destruction of large numbers of blood corpuscles.

In malarial cachexia, unless as a consequence of a recent malarial attack, melanin pigmentation is not a necessary feature. The hypertrophied condition of the spleen is largely due to thickened capsule and trabeculæ, rather than to an active congestion; the organ, therefore, is hard and tough even. In the same way the liver may be enlarged from simple congestion, or it may be in advanced cases the subject of hypertrophic or of ordinary cirrhosis. The kidneys, too, are apt to become cirrhotic, or fatty. The heart is often degenerated and dilated.

The destruction of the blood corpuscles by the proliferation and growth of the plasmodium explains, in great measure, the anæmia which is so

constant a sequela of acute malarial attacks. The fall in the corpuscular richness of the blood after even a single fever paroxysm, more especially after hæmoglobinuric attacks, is enormous, amounting sometimes to as much as 500,000 per c.mm. A very few such paroxysms, therefore, suffice to bring the blood count down to 2,000,000, or even to 1,000,000. At the same time the hæmoglobin value of the remaining corpuscles is seriously reduced.

Judging merely from the relatively scanty stock of plasmodia usually visible in the peripheral circulation, it would be difficult to account for an anæmia of so extreme and so rapidly developed a character. It must be borne in mind, however, that the principal nidus of the parasite is the blood vessels of the viscera and bone marrow, not the peripheral circulation. In these organs, as already explained, plasmodia are generally present in enormous numbers, even although they may be scanty, or, for a time, perhaps altogether wanting in finger blood.

The pigmentation of organs, so characteristic of malaria, is evidently derived from the melanin manufactured by the plasmodium, and liberated on the breaking up of the sporulating bodies. It is derived both from parasites developed locally, and from plasmodial pigment liberated in the peripheral circulation, and carried by the leucocytes to the spleen and other pigmented viscera, and there deposited. The endothelium of the vessels, as well as the white blood corpuscles, exercises a phagocytic function as regards malarial infection.

The fever in malaria is doubtless produced by a parasite-elaborated toxine liberated at the moment of breaking up of the sporulating bodies. This conjecture is countenanced by the fact that the oncoming of fever concurs, in the main, with this act in the plasmodial drama. I believe that this febrogenetic toxine, or another toxine liberated by the plasmodium, exerts a solvent action on the hæmoglobin not only of those corpuscles which harbour parasites, but also on the hæmoglobin of the other and apparently healthy corpuscles. Hence the marked diminution which is observable in the hæmoglobin value of the surviving red blood corpuscles.

The bilious symptoms, often so prominent a feature in malaria, are the result of an excessive secretion of bile; the excess of bile in its turn depending on the excess of hæmoglobin in the blood plasma. When the hæmoglobin reducing, bile forming capacity of the liver is unable to overtake the rapid and excessive liberation of hæmoglobin, a hæmoglobinæmia results. The free hæmoglobin is then deposited in the tissues, tingeing the skin and giving rise to malarial hæmatogenous jaundice. If the amount of liberated hæmoglobin be in still greater excess, it escapes by the kidneys, giving rise to hæmoglobinuria, to choking of the kidney tubules, and perhaps in this way leading to suppression of urine or to nephritis.

Symptomatology.—The incubation period in malaria is subject to very great variation. Probably eight to ten days is the minimum. The maximum may extend to years, for clinical manifestations of infection may not show themselves for a very long period after the endemic malarial region has been quitted. During the interval the parasite must lie in the tissues in some as yet unknown, passive form; the condition in these circumstances, therefore, is rather one of latency than of incubation.

Explosions of latent malarial infection may take place from time to time without very obvious cause; as a rule, however, they are generally

provoked by some physiological strain such as may be produced by chill, fatigue, excesses, injuries, mental shock, disease; in fact, by anything calculated to upset the general health, or to depress the normal powers of resistance.

Intermittent fever.—However brought about, whether by a recent or by a latent infection, the presence and active propagation of the plasmodium in the circulation are associated with certain, usually well-marked, clinical phenomena. Of these, fever of a special type is a leading one. This fever, as is the case with most of the clinical phenomena associated with the plasmodium, has a marked tendency to assume a cyclical character.

The typical clinical malarial cycle is either one of twenty-four hours, in which case it is called "quotidian"; or of forty-eight hours, when it is called "tertian"; or of seventy-two hours, called "quartan." An important pathological fact in this connection is, that these fever-cycles correspond in spacing with the life-cycles of the particular varieties of plasmodium producing them. Thus the quartan fever is produced by a parasite of seventy-two hours' cycle; the tertian, by a parasite of forty-eight hours' cycle; the quotidian, by the quotidian parasites or, more generally, by two swarms of tertian parasites maturing on alternate days, or by three swarms of quartan parasites maturing on three successive days, or by a mixed infection of quartan and tertian parasites.

The clinical cycle may be said to commence with the onset of fever. This in point of time, and doubtless of causation, corresponds with the breaking up in the blood of the sporulating plasmodia. It is signalised by a rise of temperature, headache, desire to stretch the limbs, chilliness, and the usual accompaniments of approaching febrile illness. Presently— the thermometer having already risen several degrees—violent rigor sets in, the teeth chatter, and the body becomes almost convulsed with shivering. There is cutis anserina; the pulse is small; the hands and feet feel cold to the touch, and look shrivelled; the features are blue, or pale and pinched; and pale limpid urine may be passed in large quantities. Meanwhile, notwithstanding the subjective feelings of cold characterising this, "the cold stage," the temperature in the central parts of the body —axilla, mouth, rectum—continues to rise. Vomiting may occur. After half an hour, or an hour, or even longer, the feeling of intense cold gradually gives place to one of correspondingly intense heat. The head throbs and aches; the face is flushed; the hands are hot and dry; the pulse full, quick, and bounding; the respiration hurried. Vomiting may be frequent and urgent; thirst intense. Urine is scanty and high-coloured. Occasionally there may be delirium. This, the "hot stage," may continue for two or three hours or even longer. The temperature before the fastigium is attained may rise to 104°, 106°, or even to 107° F. or over. Then perspiration begins to show itself about the neck, forehead, palms of the hands; gradually extending, it bursts out over the entire surface of the body. Sweat now literally pours off the patient, saturating his clothes and even the bedding. With the oncoming of this, the "sweating stage," febrile distress rapidly abates, the temperature falls to normal, and in the course of an hour or so the patient, beyond a certain feeling of lassitude, may find himself quite well, able in mild cases to be up and to attend to his work. During most malarial attacks the spleen becomes palpably swollen, and the liver may also be similarly affected, though to a less degree; both organs may be the seat of discomfort and even of actual pain.

The duration of one of these paroxysms of fever, which when of this

type is called "ague" or "intermittent fever," varies from three to six or eight hours, or even longer. Its degree of severity is equally variable, ranging from fever of the mildest to fever of the most intense description. The three elementary constituents of the fever fit may also vary in relative severity in different cases. Thus the rigor may be slight or severe; or the hot or the sweating stages may be similarly modified. Infinite variety obtains in this respect. Their essential characters, however, are the same whether the case be one of quotidian, of tertian, or of quartan type.

Assuming that the patient has received no efficient treatment, we will find that after an interval of complete freedom from fever, on the following, or on the second, or on the third succeeding day, and commencing about the same time of the day, an exactly similar attack takes place. For weeks these periodical attacks recur with the utmost regularity. By and by they may diminish in severity, and gradually cease; but, provided proper treatment is not instituted, and sometimes even in spite of it, relapse on slight provocation is nearly sure to occur. Occasionally, though very rarely, in a quotidian fever caused by a quartan parasite, one of the swarms of parasites may drop out; then the fever paroxysm will recur on two successive days, to be followed by a day free from fever. Or, in a quotidian ague caused by a tertian parasite, similarly, one of the swarm may drop out; then the quotidian becomes a tertian. Apparently in consequence of mixtures of the different types of parasites—"mixed infections," there is great variety in the type and course of malarial fevers, especially if owing to a recent infection. Old-standing fevers are usually typical quotidian, typical tertian, or typical quartan agues.

Fevers may tend to come on a little earlier each succeeding day; in this case the fever is said to "anticipate"—an occurrence regarded as indicative of increasing severity. On the other hand, the oncome of a fever may be delayed a little every day; the fever is then said to "postpone." This is looked on as an indication that the severity of the fever is lessening. When a paroxysm of fever is prolonged into the following day, and has not expended itself before the succeeding attack sets in, the fever is said to be "subintrant." If very little remission occurs between two fever-cycles, such an attack is called "remittent." If there be no remission in symptoms, the fever is called "continued." First attacks of malarial fever, particularly in the tropics, are apt to be of this latter character. They are generally either remittent or continued, rarely intermittent, although, on the subsidence of the more acute phenomena, they may gradually merge into a genuine intermittent fever. On the other hand, in more temperate climates, even first attacks are usually distinctly intermittent. Intermittents in the tropics are usually quotidians, that is double tertians; in temperate climates, more often tertians. Quartans are rarer both in temperate and in tropical countries; relatively to the number of cases occurring, they are proportionately rarer in the tropical than in the temperate zones. The relative proportion of tertian to quartan infections varies very much with locality and season.

Irregular and larval fevers.—Although malarial poisoning finds expression, as a rule, in well-marked ague, or in some form of so-called remittent or continued fever, yet it often happens that the presence of the plasmodium in the blood is not so acutely or definitely signalised. Feverishness with slight or well-marked elevations of temperature, accompanied by greater or lesser degrees of lassitude, headache, anorexia, splenic enlarge-

ment, anæmia, coming and going at short but somewhat irregular intervals of a day or two, or it may be at longer or more or less regular intervals of one, two, or three weeks, may be all the clinical evidence of plasmodial infection. The parasite in such cases can generally be found in the blood, even during apyretic intervals of considerable duration. Any depressing or exhausting circumstance, such as exposure, or irregularity of living, and so forth, tends to favour a more active proliferation of the plasmodium, and consequently more acute clinical manifestations.

Ordinary agues, remittents and continued malarial fevers, although sometimes giving rise to extreme debility and anæmia, do not seriously endanger life. Occasionally, however, in the subtropics, but more particularly in the highly malarious districts of the tropics, and especially in the case of infections by the crescent-forming, small-spored plasmodia, malarial disease may assume a grave and even malignant character. These cases form an important clinical group, which is divisible roughly into bilious remittent, typho-adynamic, and pernicious fevers. The pernicious fevers are sometimes classified into cerebral and algid; the latter being character-ised by suddenly developed adynamic symptoms and a tendency to collapse, the former by various symptoms attributable to grave implication of the brain and nervous system.

Bilious remittent.—This type of malaria, besides being accompanied by the usual remitting or more or less continued fever, is specially charac-terised by symptoms indicating severe implication of the abdominal viscera. There is a great amount of epigastric discomfort; marked enlargement of the spleen; slighter enlargement of the liver; a somewhat swollen, thickly-coated tongue; much nausea; much vomiting of dark bilious material; severe headache; thirst; anorexia; an icteric tint of skin and scleræ; sometimes constipation, sometimes bilious diarrhœa. The acute symptoms under proper treatment slowly or more quickly subside in the course of a week or ten days. If left to itself, the disease may spontaneously and slowly subside; or it may merge into an ordinary intermittent, or into the following:—

Typho-adynamic fever.—In this the symptoms assume a typhoid character. They may be asthenic from the outset, especially in the debilitated and cachectic; or, having commenced as an ordinary remittent or intermittent, the sthenic symptoms after a time give place to those of a typhoid and asthenic type. The patient is extremely prostrate. There may be low, muttering delirium; hallucinations; catching at imaginary objects; picking of the bedclothes; subsultus; dry tongue; sordes in the mouth; a feeble, running, perhaps dicrotic pulse and other indications of the typhoid state. Such fevers are highly dangerous; collapse, or more active pernicious symptoms, may at any time suddenly supervene. They are apt to be complicated by a low and very dangerous type of pneumonia, or with bedsores, or other form of gangrene.

Pernicious attacks may occur in the course of what are apparently ordinary, and perhaps by no means severe, malarial fevers. Their dis-tinctive marks are suddenness of onset and gravity.

The pernicious nature of the attack seems to depend on a variety of circumstances—(1) Embolic plugging of the capillaries and small arteries of important organs by accumulations of plasmodia. (2) A large dose of plasmodial toxine in the presence of a special susceptibility depending either on personal idiosyncrasy; or on lowered resistance from intemperance, hardship, other diseases; or, and especially, on previous malarial attacks.

(3) A special type of plasmodium; or a second and superadded infection by fresh malarial or other and as yet unknown germs.

To the first category may belong hyperpyrexial, comatose, convulsive, paralytic, gastric, choleraic, and dysenteric attacks; to the second, syncopal and colliquative attacks; to the third, hæmoglobinuric attacks.

Hyperpyrexial, comatose, convulsive, and paralytic attacks.—It occasionally happens in the hot stage of what appears to be an ordinary intermittent or remittent, and without obvious reason, that hyperpyrexial temperature is rapidly attained. In malarial fevers, high temperatures, 106° or 107°, are not uncommon; provided they are not long maintained, these temperatures are not specially dangerous. Beyond this point, however, there is grave risk to life. On the thermometer reaching 106° or 107°, the patient is apt to become delirious; on its attaining 108° he may become for a short time wildly maniacal, and then rapidly lapse into profound coma with stertorous breathing, a flushed and bloated face, and a full and bounding pulse, which rapidly loses its sthenic character, and, becoming weak, flutters and stops. Frequently at the time of death temperatures of 110°, 112°, or even higher, are registered. Those hyperpyrexial malarial attacks are liable to be misunderstood, and are often called "sunstroke," "heat apoplexy," or "ardent fever"; this is a serious mistake if the diagnosis should imply a treatment in which quinine in full doses promptly administered is not included.

Although delirium, coma, and convulsions are common in hyperpyrexial attacks, they may also supervene in fevers in which there is no unusual or excessive elevation of temperature. Similarly, aphasic symptoms of a transitory nature, amaurosis of central or peripheral origin, and other forms of cerebral paresis, are occasionally met with. The leading feature in these cases seems to depend on the particular cerebral centre picked out by the embolic plasmodia.

Algid attacks.—These may supervene during what in point of time would be the hot stage of an intermittent. The patient does not react after the cold stage. He does not suffer, but he is profoundly prostrate. The skin has a frog-like feel, being cold and covered with a clammy sweat. The tongue and breath are also cold; the pulse is rapid and small; the temperature little, if at all, raised. These attacks are highly dangerous, and are prone to end in fatal asthenia.

Diaphoretic attacks.—In these the terminal sweating of an ague is very much exaggerated, prostrating the patient and rendering him liable to alarming collapse, or to syncope on rising from bed or on making the slightest effort.

Choleraic attacks may occur during either the cold or the hot stage. There is sudden and profuse vomiting and diarrhœa, a choleraic countenance and voice, suppression of urine, and, very often, cramps in the calf muscles. At times the attack ends in fatal collapse. The stools are always to some extent bilious, and do not assume the true rice-water appearance of the stools of true cholera.

Dysenteric attacks.—These may occur in the course of an ague fit, blood being passed in considerable quantities together with a certain amount of mucus. Tenesmus and the usual subjective signs of dysentery may also be present. The temperature is higher than it usually is in the acute stage of true dysentery—a circumstance which, together with the history, should put the physician on his guard in diagnosis.

Hæmoglobinuric fever.—In certain parts of the tropical world, and

in some malarial spots in more temperate zones, but more especially in tropical Africa, a form of what is generally regarded as malarial fever is found, to which the names of "blackwater fever" or "haematuric fever" are commonly applied. In tropical Africa this disease is one of the commonest causes of death in Europeans, amounting to a scourge in many parts of the West Coast, on the banks of the Congo, and on the Niger; it also occurs in Nyassaland, in Mozambique, on the Zambesi, and in many parts of the East Coast. It is common in Madagascar. It is very rarely heard of in India, but it occasionally occurs in Assam, Cochin-China, Java, New Guinea, and probably elsewhere in the Eastern Hemisphere. It occurs also in the West Indies, in the Southern States of the Union, in Colombia, and in Central America. It is occasionally met with in South Italy, Sicily, and Greece.

The patient has usually been in malarial regions for a considerable time, and has suffered much from malaria, and very probably is anæmic and debilitated. During the course of what he at first regarded as one of his familiar fevers, he feels an urgent desire to pass water. He notices that his urine has become very dark—like Malaga wine. About the same time that the urine becomes discoloured, he notices, or his friends remark, that his skin and scleræ have assumed a deep saffron-yellow colour. Vomiting of dark bilious matter sets in. He suffers from bilious diarrhœa, or, it may be, from constipation. There is severe pain in the liver, spleen, epigastrium, and loins. This condition after a time may subside, the urine, within a few hours, becoming clear on the defervescence of the fever. The disease may now stop. Or, after temporary cessation, the hæmoglobinuria, epigastric distress, and other symptoms may return with the next fever fit. On the other hand, all the symptoms may persist; there being no remission, the patient continues feverish and to pass black-brown urine in great abundance, or, it may be, in gradually decreasing amount. In the latter case the secretion may be reduced to a few ounces of a dark gummy material, or it may be entirely suppressed. The spleen and liver, during the attack and afterwards, are enlarged and very tender. A profound anæmia and great prostration are rapidly induced.

Death from this disease is very common—a large proportion, equalling at least 25 per cent., of the attacks proving fatal. Death may occur from asthenia during, or soon after, the attack; from syncope; from uræmia consequent on suppression; or from nephritis at a somewhat later period. In the majority of cases the threatening symptoms clear away rapidly or more slowly; but if the patient remain in the malarial district, he is prone to a recurrence of all the symptoms during some subsequent attack of fever.

The urine is characteristic. On standing, a copious deposit forms, which chemically, with the polariscope, and under the microscope, shows all the characters of slightly altered hæmoglobin. It often includes many hæmoglobin tube casts, and much brown, amorphous, granular material; but there are no, or very few, red blood corpuscles. The urine is highly albuminous during the height of the attack; and albumin in gradually diminishing amount may be found in it for several days after the colour has become normal and hæmoglobin has entirely disappeared.

One attack of this disease powerfully predisposes to subsequent attacks. It rarely occurs in new-comers, being most frequent about the third or fourth year of residence in the endemic area. Those who have suffered in the tropics may have a relapse after their return to Europe, and may even

die of the same; it would seem, however, that once arrived in a temperate climate, the tendency to attack ceases after four or five months. In the endemic area, the slightest chill or physiological strain is apt to bring on an attack in the susceptible. The natives suffer occasionally from hæmoglobinuric fever, but with them it is a very rare occurrence.

There is strong evidence for believing that in certain idiosyncrasies quinine is the most potent determining cause for the explosion of hæmoglobinuric attacks; a special type of malaria parasite preparing the blood for the cataclysm.

It is believed by some that this disease is of comparatively recent introduction into Africa, and that it is yearly becoming more common there. Until quite recently, it appears to have been unknown, at all events it was undescribed in India. A small variety of plasmodium, as well as benign tertian parasites, have frequently been found in the blood, but their exact characters, as yet, have not been fully determined. Yersin says that he has found a special form of bacterium in the urine, a bacillus which he is inclined to regard as having a bearing on the pathology of the disease. This observation has not been confirmed.

From clinical and epidemiological considerations, I have been led to regard the parasite of hæmoglobinuric fever as being in some respects different from that of ordinary malarial infections. Recently Sambon suggests that it is similar to *Pyrosoma bigeminum*, the parasite giving rise to Texas cattle fever, a parasite which is transmitted through the cattle tick, *Ooaphilus bovis*.

Malarial cachexia.—In consequence of severe, or of prolonged, or of frequent attacks of malarial fever, and also of long residence in malarious localities, a characteristic cachexia may ensue. All malarial attacks eventuate in more or less anæmia. In fevers caused by the benign non-crescent-forming parasites, quartan or tertian, provided the cases are properly treated, the anæmia as a rule quickly disappears; but after infections by the malignant, small-spored, crescent-forming parasites, and also in untreated benign infections, a very definite and characteristic cachexia of a more permanent character is to be expected.

The intensity of this cachexia differs in different individuals. Besides the anæmia and its usual accompaniments of vertigo, tinnitus, lassitude, liability to œdema of the legs, retinal hæmorrhages, and so forth, malarial cachexia is invariably accompanied by enlargement of the spleen—often to an enormous extent, the organ descending to the crest of the ilium, stretching well to the right of the umbilicus, and sometimes almost filling the abdomen. In many cases the liver also is swollen, but, as compared to the spleen, to a much smaller extent. Other features of this cachexia are a peculiar, sallow, earthy, subicteric colour of skin; dirty yellow sclerotics; proneness to ulceration after slight injury—especially of the legs; tendency to a scorbutic-like condition of the gums; hæmorrhagic complications, such as bleeding from the gums, nose, bowel, and small hæmorrhagic effusions into the skin, especially around insect bites; liability to catarrhal affections of the alimentary canal; irregular attacks of slight or severe fever; and, generally, the presence of some form of the plasmodium —more especially of the crescent body—in the blood. The reproductive powers are said to be very much impaired.

Although cases are on record in which a mother, reputed to be the subject of malaria, gave birth to a child with an enlarged spleen and other evidences of intra-uterine malaria, so far there has been no such instance

in which the diagnosis was confirmed by a microscopic examination of the blood. In the immature, the cachexia tends to retard development and to postpone the advent of puberty.

In recent cases, the spleen, by suitable treatment, can be reduced in size, often completely; but in cases of long standing, the hypertrophy, depending as it does in great part on fibrous changes in capsule, trabeculæ, and parenchyma, is permanent. In many malarious districts nearly every inhabitant is the subject of this form of enlargement of the spleen—"splenic tumour," as it is called. This fact has two very important practical bearings. First, the relative frequency of splenic tumours in a district is a convenient indication of its salubrity, or the reverse. Second, these spleens are readily ruptured by slight violence; consequently, in the natives of those districts, violent games, corporal punishment, or anything which is likely to eventuate in a blow over the spleen, are to be carefully avoided.

Malarial cachectics are prone to attacks of intermitting, quotidian, or tertian neuralgia, especially in the supra- or infra-orbital nerves. They are also liable to headaches, gastralgia, vomiting, and attacks of palpitation. Pneumonia is likewise a common and highly dangerous occurrence with them, and so are dysentery and diarrhœa.

Diagnosis.—Apart from such considerations as history and locality suggest, the diagnosis of malarial disease hinges principally upon four points —(1) periodicity; (2) enlargement of the spleen; (3) the action of quinine; (4) the presence of the plasmodium or its product—melanin—in the peripheral circulation. With the exception of the last, none of these is infallible as a test for malaria. Unfortunately, as affecting the microscopic method of diagnosis, negative results from an examination of the blood, particularly if made after the administration of quinine, are not of the same value in deciding against, as positive results are in indicating, the presence of malarial infection.

Periodicity, particularly tertian or quartan periodicity, is a valuable sign of malaria. It must be remembered, however, as affecting the diagnostic value of quotidian periodicity, that most febrile processes, particularly such as are associated with suppuration—abscess of the liver, for example—are sometimes in regularity of rhythm remarkably like malarial fever; so is that fever which is sometimes associated with gallstones, with surgical kidney, with urethral disease, with tuberculous processes, and so on. An intermittent quotidian fever setting in early in the day and having its fastigium before late afternoon, is probably malarial; septic fevers, as a rule, have their fastigium later in the day or during the evening or night. Tertian and quartan periodicity, when pronounced, are peculiar to and absolutely diagnostic of malaria.

Enlargement, of the spleen, if absent, tells against a diagnosis of malaria; but its presence in connection with a recurring or intermittent fever is by no means pathognomonic of malaria. This type of fever and splenic tumour are found concurring in many other diseases—splenic leucocythæmia, pernicious anæmia, Malta fever, for example.

The action of quinine in intermittents and in many irregular malarial fevers is usually so prompt and decided, that it supplies one of the most valuable tests of malaria we possess. In remittents, however, its action is not generally so marked or prompt. In pernicious attacks it is of little practical value as a diagnostic, seeing that diagnosis in these cases, to be of use, must be made at once and before quinine could have time to act.

In hæmoglobinuric fever, quinine, whether from the standpoint of diagnosis or of treatment, seems to have little or doubtful value.

Presence of the plasmodium.—By far the most valuable indication of malarial disease is the discovery of plasmodia or their product, melanin, in the blood. A microscopical examination of the blood should therefore be made in every case in which the slightest doubt exists; if possible, it should be made before quinine is administered, as this drug causes most of the forms of the plasmodium—all, in fact, except the crescent body and its derivatives—to disappear rapidly from the circulation. Fresh wet preparations should be examined first; if the result from these is negative, and for greater security, stained preparations should then be examined.

The following procedures are well adapted for demonstrating the plasmodium. Cleanse very thoroughly several slips and cover-glasses with alcohol; cleanse a finger-tip in the same thorough way. Prick the finger with a clean needle. Express from the puncture a small quantity of blood; this, as it may contain epithelium detached by the needle, should be wiped away with a clean cloth. Express from the same puncture a second droplet, about as large as a pin's head; touch the apex of this lightly (taking care not to impinge on the skin) with the centre of a cover-glass, and lay the cover-glass on a slip. If glasses and finger are clean, the blood will at once run out in an exceedingly delicate film in a considerable area, of which the corpuscles lie flat, isolated, and slightly expressed. After waiting about a minute for the blood film to spread out, it is well to ring the cover-glass with vaseline, to prevent evaporation and consequent crenation, movement, and excessive compression of corpuscles. Using a twelfth of an inch immersion objective, and a good but not too brilliant illumination, search is made in those parts of the film in which the blood corpuscles are lying isolated and flat. Each corpuscle is separately scrutinised, the observer looking carefully for any indication of black pigment, or of a pale, nebulous, amœboid body lying in the hæmoglobin. There is little difficulty in recognising the larger forms of the highly pigmented intracorpuscular bodies, the rosette bodies, the crescents, the crescent-derived spheres, and the flagellates; but it is sometimes very difficult, at all events for the novice, to recognise the smaller and unpigmented phases of the plasmodium. When doubt exists about some intracorpuscular appearance, the detection of amœboid movement is a valuable aid. Vacuoles must not be mistaken for plasmodia; the former are clear, sharp in outline, and non-amœboid, and of course do not take a stain; the latter are nebulous, with ill-defined outlines, often amœboid, and readily take the methylene-blue stain after fixing with alcohol or heat. Certain of the minute plasmodia tend to assume a ring form, which is very characteristic; although minute, these rings are clear, well defined, and not difficult to recognise. They are sometimes seen in very dark, shrivelled corpuscles, called from their colour "brassy bodies"; such are frequent in malignant infections. Pigmented leucocytes are easily made out, and are quite as pathognomonic of malaria as the actual plasmodium itself. In seeking for plasmodia, the novice must bear in mind that rosette bodies and flagellates are not always, or even generally, present; in fact, they are only to be found at particular times in the case of the former, and only some time after the slide has been put up in the case of the latter. The usual forms encountered are the smaller or larger unpigmented or pigmented intracorpuscular phases, crescents, and crescent-derived ovals and spheres. To find flagellates, it is best to select a crescent case, and, as Ross

has pointed out, to expose the droplet of blood to the air for two or three minutes before making the preparation; if the slide be examined from fifteen to twenty minutes later, and the crescents have been present, a considerable proportion of them will now be found transformed into flagellates.

In those parts of the preparation in which, from compression, the blood corpuscles have been ruptured, fragmented plasmodia, or even entire plasmodia, are often seen free in the liquor sanguinis. These bodies are generally spherical or discoid, and contain innumerable particles of fragmented melanin dust, or protoplasmic granules in active Brownian movement.

To prepare stained films, the following plan will be found serviceable. Provide a piece of tissue paper, or, better, of guttapercha tissue 2 in. long by 1 in. broad. Prick the finger and express a droplet of blood in the usual way. Take the blood up on one face of the guttapercha tissue, near one end. Lay the tissue on a slip, and, after pausing for a few seconds to allow the blood to run out in a film between it and the slip, draw the former horizontally along the slip; a very fine and often beautifully uniform film is the result. This, after it has dried, is fixed by pouring on it a few drops of absolute alcohol; five minutes suffice. It is then dried again, and the stain—2 per cent. methylene-blue, 5 per cent. borax in distilled water—is dropped on the film. After thirty or forty seconds the preparation is thoroughly washed, dried, and mounted in zylol balsam. The microscopical examination should be made with a twelfth of an inch immersion lens. The parasites (Fig. 39) are readily recognised by their blue tint; by the fact that they are lying in red blood corpuscles; by the presence of black pigment in the interior of the larger plasmodia; and, in the case of most of the immature plasmodia, by the large, unstained, and very apparent vesicular nucleus, usually containing a minute, deeply stained, and eccentrically placed nucleolus. The smaller parasites appear in such preparations as minute, delicate, blue rings surrounding the un-stained vesicular nucleus, which almost invariably carries a very apparent, deeply stained, eccentrically-placed nucleolus. Crescents and sporulating forms are easily recognised. There should be no difficulty in distinguishing the plasmodium from the leucocyte, as the nuclei of the leucocytes are deeply stained, whilst those of the parasite are unstained; the former have no setting of hæmoglobin; moreover, the peripheral protoplasm of the parasites, though less deeply stained than the nuclei, is more deeply stained than the protoplasm of the leucocytes.

There are many other methods of staining malarial parasites, but none so easy of application, or which give better results, than those processes in which methylene-blue is the staining agent. Eosin or safranin may be used as counter-stains. They are not necessary.

To stain the flagellated bodies, I recommend the following:—Select a case in which crescents are numerous. Prepare a moist chamber by cutting an oblong hole in a piece of thick blotting-paper, which is then moistened and laid on some non-absorbent flat surface. Take a small droplet of blood upon the centre of a slip, and spread it out quickly with a needle. Immediately place the slip over the moist chamber. After half to three-quarters of an hour, remove the slide; dry it quickly; fix with alcohol; remove hæmoglobin by immersing for half an hour in weak (20 per cent.) acetic acid; wash well; stain for six hours in 30 per cent. carbol-fuchsin; wash; mount in xylol. Beautiful preparations may be obtained in this way.

It must never be forgotten that malarial fever is prone to complicate other diseases, such as enteric fever, phthisis, the various forms of anæmia, dysentery, and so forth. Under such circumstances a microscopical examination of the blood is invaluable.

Prognosis.—Although the mortality from malarial disease as compared to the number of attacks is small, yet, on account of the great frequency of this infection, the aggregate mortality is very large indeed. In India, for example, the deaths from malaria far exceed those from cholera or any other disease. Ordinary uncomplicated intermittents or remittents, as immediately affecting life, are of little gravity; but as they are always followed by more or less anæmia, and are nearly certain to recur, they generally give rise to much debility and very frequently to various abdominal or other complications. In this way, doubtless, they predispose to other disease, and are a fruitful indirect cause of death.

The prognosis depends in great measure on the treatment employed and the hygienic conditions of the patient. Liberal but judicious dosing with quinine, good food, and change to a salubrious district, usually mean speedy recovery; no quinine, indifferent food, and continued residence in a malarial district, mean relapse, and sooner or later forms of malarial cachexia.

Pernicious attacks are always dangerous, particularly if not promptly recognised and properly treated. The mortality in such attacks amounts to about one in three. Infections of the small crescent-forming parasite are much more dangerous than those from the benign tertian or from the quartan plasmodia. They are also more prone to recur, more often followed by cachexia, more liable to assume pernicious characters, and are less amenable to quinine. Because the smaller type of parasite prevails especially in autumn, and the benign parasite more particularly in the earlier part of the year, autumn malaria is usually more serious than spring attacks. Great differences are observable in malaria according to the locality in which it is acquired; thus West African malaria, as a rule, is infinitely more dangerous than the malaria of Europe or even of India.

Treatment.—The treatment of malarial disease means the administration of quinine. For ordinary cases I make it a practice to give 10 grs. of the sulphate so soon as the sweating stage is well established, and thereafter 5 grs. three times a day for three or four days. The drug is said to act most effectively on the young forms of the plasmodium, and it is these forms that predominate, or are perhaps the only form present, during the sweating stage. With a view to prevent relapse, I generally recommend that three 5-gr. doses be taken one day each week—that is, every seventh day—during from six consecutive weeks to three months, a mild saline purgative being administered in the early morning of the same day. Agues rarely resist this treatment. Although quinine acts most efficiently when given shortly before the commencement of the paroxysm, unless in the presence of threatened danger it is not advisable to give it at that time or during the cold or hot stages; given then it is apt to aggravate headache, and it has no influence in cutting short the impending or current attack. But in continued fevers, or in the presence of danger, quinine should be given at once in 10-gr. doses every six hours or oftener, and irrespective of the stage of the disease

In agues, quinine, when efficiently administered, very often stops or powerfully modifies the following attack; almost invariably the second

following attack does not come on. When the stomach is irritable and there is much vomiting, and when such a case is not deemed grave, quinine may be given in enema. The dose in this case should be double of that given by the mouth. Before administering it, the bowel must be washed out by a simple enema. In serious fevers, and when the tongue is foul, and there are evidences of gastric catarrh and debilitated digestion, the drug should be given in solution. When the tongue is clean, freshly made quinine pill, or the powder in cachet, tabloid, or milk, are less unpleasant to take, and are absorbed readily enough.

Important accessories to treatment by quinine are rest, warmth, and good food. These alone sometimes suffice to bring about the cessation, for the time being at all events, of the active manifestations of malaria. I have often watched the gradual disappearance of the plasmodium from the blood, and of the associated recurring febrile attacks, under their influence alone, and without a grain of quinine having been swallowed.

In the presence of severe malarial attacks attended with vomiting, and particularly when a pernicious attack is impending, or has developed, the quinine must be given hypodermically and in full and repeated doses. Owing to its great solubility in water, and to its containing more of the alkaloid than the sulphate, the acid hydrochlorate is the best salt for hypodermic injection. The following is a good solution for hypodermic purposes:—Acid hydrochlorate of quinine, 5 grms.; distilled water, 10 c.c. Of this 1 c.c. is equal to $\frac{1}{2}$ grm.—7$\frac{1}{2}$ grs.—of the salt—a sufficient dose in ordinary cases, but which in severe or in pernicious cases has to be doubled and administered at least thrice a day. In the absence of the acid hydrochlorate the ordinary commercial hydrochlorate can be used, a little hydrochloric acid, or one-fourth part of its weight of antipyrine, being added to aid solution. The latter injection is said to give good results. Sometimes neither of the hydrochlorates are procurable; in that case the sulphate must be employed, solution being effected by the addition of half its weight of tartaric acid. In using hypodermic injections of quinine, great care must be exercised to secure a perfectly aseptic condition of the instruments, the solution, and the skin. The instrument and solution should be boiled; only a filtered and clear solution should be used; and the skin must be thoroughly cleansed. The injection should be made deep into the subcutaneous tissue and not into the derma, the eye of the needle being directed away from the skin. Some prefer to inject deep into the body of a muscle to injecting close under the skin; it is much less painful. Abscess, ulcers, and ugly scars have sometimes resulted; and more than once lives have been lost from tetanus after quinine injections. Such mishaps are almost entirely attributable to the use of dirty syringes and solutions.

Baccelli, in certain malignant and almost desperate cases of malaria, has employed successfully intravenous injections of quinine. His prescription is:—Hydrochlorate of quinine, 1 grm.; chloride of sodium, 75 cgrms.; distilled water, 10 grms. By means of a Pravaz syringe, half of this quantity, slightly warmed, is injected into a vein. The needle should be thrust well into the distended vein, and injection made in the direction of the circulation.

In severe remittents, in continued malarial fevers, and in pernicious attacks, besides administering quinine, which is invariably the first and most important duty to be attended to, certain symptoms may require special treatment. In bilious remittents attended with excessive vomiting,

sinapisms to the epigastrium, a full dose of calomel or sometimes of ipecacu-anha, and afterwards, if necessary, a small hypodermic injection of morphine, are often effective in allaying sickness; effervescing drinks or sips of very hot water are also useful in these circumstances. In pernicious attacks of an algid character, frictions with camphor and spirit; ether or strychnine by the mouth or hypodermically; hot bottles to the extremities; cham-pagne, and other alcoholic stimulants, are all sometimes of service in stimulating the circulation and procuring reaction. In hyperpyrexia, efforts to reduce and keep down temperature must be prompt and energetic; cold sponging, ice to the head, iced enemata, or, better, continuous immersion in a cool bath, the temperature of which is gradually lowered and regulated by ice or cold water, are indispensable. Pending the specific action of hypodermic injections of quinine in 10-gr. doses, repeated hourly for two or three times if necessary, it is imperative to lower and keep down temperature, otherwise the patient will surely die. Ordinary antipyretics, such as antipyrine, phenacetin, etc., are useless or even dangerous in per-nicious attacks, although they are of distinct service in relieving headache in the milder malarial fevers.

The most opposite opinions are entertained in regard to the treatment of hæmoglobinuric fever. Some advocate quinine in full doses, 20 to 30 grs. repeated two or three times a day; some recommend it in moderate doses, 5 to 10 grs.; others, again, have discarded this drug altogether, in the belief that it aggravates the hæmoglobinuria. Calomel in large doses is much in vogue for this type of malaria in Africa. Certain French writers have lately advocated chloroform—5 to 6 minims in water every ten minutes, till a certain degree of chloroform intoxication is produced, the effect being subsequently kept up by chloral. Tannin has also a certain reputation in hæmoglobinuric fever, as well as in other forms of malaria; it is given in 15-gr. doses, in sweetened water, every eight hours. The subject of one attack of hæmoglobinuric fever should, if at all possible, quit the endemic area, otherwise relapse on the slightest exposure or strain is almost certain, and then the risk to life is very great. Such patients, however, must be careful to avoid returning to Europe in the late autumn, winter, or early spring, for it often happens that a sudden and premature plunge into cold weather provokes an attack which may prove fatal; such patients should winter at the Canaries or in Egypt.

For the anæmia succeeding malarial attacks, arsenic combined with iron and small doses of quinine or nux vomica is the best remedy. It must be supplemented by good food, a little generous wine, warm clothing, and, if possible, a dry, sunny, and not too cold a climate. Mountain air or a sea voyage are excellent restoratives.

For the congestions of liver and spleen, and the chronic intestinal catarrhs—so common a sequela of malaria—there is nothing more effica-cious than a course of Carlsbad. If it is impossible to visit Carlsbad, a fair substitute for the waters and the treatment practised there is as follows:—Dissolve 53 grs. of Carlsbad salt in a pint of very hot water; divide this into three equal portions; the three portions are sipped hot and slowly, at intervals of twenty minutes, the first thing every morning and on an empty stomach. Food must be light and digestible; milk, fat, cheese, fruit, wine and beer, and all indigestibles being avoided. The course should be kept up for three weeks.

If enlargement of the spleen persist after a malarial attack, it may be treated by counter-irritation with liniment of iodine, and with mild warm

saline aperients and quinine. Arsenic and iron, electricity, carefully applied hot and cold water douches, and *gentle* massage are all useful at times. Whenever practicable, the subject of repeated malarial fevers should leave the endemic district, and, if possible, return for a time to Europe.

Many substitutes for quinine have been suggested and tried. Amongst others may be mentioned arsenic in very large doses, strychnine, chiretta, iodine, alum, tannin, methylene-blue, anarcotin, phenocol, analgen, carbolic acid, etc. None of these, however, approach quinine in efficacy. What is known as Warburg's tincture, and which contains a large number of diaphoretic drugs, and also a considerable quantity of quinine, is much used in Indian practice. The dose is half an ounce, to be repeated at the end of two or three hours. Warburg's tincture generally brings on profuse diaphoresis. It has sometimes succeeded where quinine alone had failed apparently. This must be based on the fact that the mosquito is the transmitting agent of the malarial parasite.

Prophylaxis.—Much can be and has been done by efficient drainage and careful cultivation to extirpate mosquitoes, and so to render malarious countries healthy; unfortunately, much has also been done by the artificial irrigation of previously dry and healthy countries to render them malarious. As an example of the former, the case of the fen country in England may be quoted; of the latter, the unhealthiness which has succeeded irrigation works in many parts of India.

The sites of dwelling-houses in malarious districts should always be carefully selected, rising ground being preferred to a valley. Dwelling-rooms, especially bedrooms, should be well raised above the ground. Mosquito nets are indispensable. The neighbourhood of the residence should be drained and covered with well-kept turf, or cultivated. All puddles should be filled in with earth, or drained, or kept covered with a film of kerosene oil, a few ounces of which quickly rid a pool or pond of its mosquitoes. Districts in which many of the inhabitants have enlarged spleens must be avoided as places of residence. If there be an option, a town residence, after the town has been built for several years, is decidedly preferable to a suburban or country one; but during the building of a town, and for some years afterwards, the open country is the safer. Journeys and campaigns in malarious districts ought not to be undertaken during the fever season.

There has been considerable difference of opinion with regard to the prophylactic virtues of quinine. General experience, however, is now decidedly in favour of its systematic use with this object—at all events, during journeys or temporary residence in malarious countries. Three to five grs. once a day, or two or three 5-gr. doses in one day once or twice a week, may be taken. Arsenic is of no value as a prophylactic.

In malarial countries, great care should be exercised to preserve the general health. Regular exercise; temperance in eating and drinking; sufficient but not exhausting occupation; cheerfulness; the avoidance of chill, of constipation, of exposure to the hot sun and of late hours, of mosquito bites, of being out of doors before sunrise or after sunset,—these common-sense matters ought to be rules with all residents in such districts.

Earth-cutting operations are particularly dangerous, and should be avoided during the fever season; those employed ought never to sleep in the neighbourhood of such works.

PATRICK MANSON.

GENERAL GONORRHŒAL INFECTION.

BESIDES the direct extension of the gonorrhœal process to the adjacent tissues, serious complications, such as cystitis and pyelitis, may arise by continuity; while in women, metritis, salpingitis, ovaritis, and peritonitis have also been found. In addition to such effects, a general infection of the system may take place, and produce widespread effects.

Ætiology.—The gonococcus has been found in the blood and in the internal organs, sometimes alone and at other times associated in a mixed infection with streptococci and staphylococci. The source of the infection is not always the urinary tract, since it has been found to take place as a sequel to gonorrhœal conjunctivitis.

Morbid anatomy.—Where general systemic infection has occurred, there is commonly one definite seat of suppuration, *e.g.* an abscess in some part of the urinary tract or its annexa. The pathological results depend on the distribution of the disease. In gonorrhœal synovitis there is effusion into the affected joint; this is rarely purulent, but contains gonococci, often yielding a pure culture. There is often considerable periarticular inflammation, and the sheaths of the tendons in the neighbourhood may be implicated. When gonorrhœal endocarditis and pericarditis have been set up, the characteristic lesions are found after death, often associated with changes in the muscular wall of the heart, and the gonococci are found alone or combined with other organisms.

Symptoms.—As the result of general infection, a condition of profound toxæmia has been found, and the patient, as in a case narrated by Osler, passes rapidly into a typhoid state, and dies, apparently from general sepsis.

The most usual clinical condition is gonorrhœal synovitis. It is almost always met with in males, and only rarely in females. Usually one joint, the knee or ankle, is first involved, but others may be involved in succession. Certain joints, which are seldom affected by rheumatism, are fairly frequently the seat of gonorrhœal infection, namely, the sterno-clavicular, the temporo-maxillary, the intervertebral, and the sacro-iliac joints. The actual amount of effusion into a joint is not great as a rule, but a good deal of œdema occurs around the joint, and some effusion into the adjacent tendon sheaths. The joints are extremely tender on pressure, and the synovitis is apt to persist for some time. Probably, on account of the slow recovery, there is a tendency to the formation of fibrous adhesions; and if repeated attacks occur in the same joints from fresh gonorrhœal infections, fibrous ankylosis may result. The ankylosis, as in a terrible instance mentioned by Fagge, may affect every joint in the body.

In gonorrhœal endocarditis the symptoms are those of a septic condition, and physical examination may or may not reveal the cardiac mischief. The course of this complication is that of acute endocarditis, sometimes presenting the *typhoid type*, and in other cases the *intermittent*. When gonorrhœal pericarditis sets in, it gives the clinical features of that affection.

Diagnosis.—Synovitis occurs as a symptom of or a complication or sequela of many diseases. Its association with rheumatism, rheumatoid arthritis, and gout will be fully dealt with in the sequel. It is very apt to follow injury of almost any kind to a joint; it is very frequently secondary to a general tuberculosis, and is then the result of a tuberculous affection of the synovial membrane; it is an occasional sequela or complication of the

various infectious fevers, of dysentery, and of pyæmia; it is associated with syphilis, especially in its later stages; and a special form of synovitis may occur in connection with locomotor ataxy, chronic disease of the spine, and occasionally with acute myelitis. All these possibilities have to be borne in mind before forming a diagnosis. The different infections leading to cardiac complications must also be considered in dealing with endo-cardial affections. The history of the case, and its intractability to ordinary means of treatment, may also be of diagnostic import.

Prognosis.—It is scarcely possible to formulate definite statements with regard to this aspect of the subject. In simple arthritic compli-cations the prospect for the patient is favourable in the main, although the duration of the disease may be prolonged. When cardiac complications supervene, the prognosis is very grave.

Treatment. — Salicylates are of no use in the treatment of gonorrhœal synovitis. Rest should be enjoined, and cold applications to the joints will effect some relief of the pain, but probably greater relief is obtained by the use of radiant heat or superheated air. Iodide of potassium, in combination with iron and quinine, should be given internally. Suitable treatment for the gonorrhœal discharge must necessarily be em-ployed. If the arthritic trouble is slow to subside, incision and irrigation of the affected joints may be necessary. When ankylosis takes place, the adhesions must be broken down under an anæsthetic. For gonorrhœal endocarditis the treatment applicable to endocarditis must be employed. Probably, in the near future, remedies which are distinctly antidotal will be found.

<div align="right">A. P. LUFF.</div>

SYPHILIS.

SYPHILIS is an infective, specific disease, of slow evolution and long duration; either acquired by inoculation, or inherited from a parent affected by the same malady. The acquired form is characterised by a primary lesion, followed, after an interval, by constitutional symptoms, along with affections of the skin and mucous membranes, and commonly at a still later period by disorders of the viscera, bones, blood vessels, skin, etc. The inherited form exhibits similar symptoms, with the exception of the primary lesion. The disease, as a rule, cannot be re-inoculated on a person who has once been infected.

History.—Syphilis has probably existed in its present form from the earliest times, but it was not until about the end of the fifteenth century, when it appeared in Southern Italy in an epidemic form, that it was recog-nised as a distinct disease. It was at that time erroneously thought to be a new disease which had been introduced from America, then just discovered. For long, syphilis was confused with other forms of venereal disease, such as gonorrhœa and soft chancre; and it was not until the nineteenth century that it was completely dissociated from these maladies.

Etiology.—Although a specific micro-organism has not been dis-covered in syphilitic lesions, there is little doubt that the disease depends, like tuberculosis, on some parasitic microbe. Lustgarten (1884) described a bacillus which he found in sections of tissues involved in syphilomata and in the pus from hard chancres. It was $3.5\,\mu$ to $4.5\,\mu$ in length, and resembled the tubercle bacillus in appearance and staining reaction.

This bacillus seems to be identical with the smegma bacillus, so frequently present in the secretion of the prepuce or vulva. There is no satisfactory experimental evidence that Lustgarten's bacillus has any causal relation with the disease. The same may be said of the bacillus described by Eve and Lingard (1886), the micrococci of Disse and Taguchi (1886), and the bacillus of Golasz (1894). Van Neissen (1899) claims to have obtained and cultivated a bacillus similar to that of Lustgarten.

Syphilis appears to be a disease peculiar to the human race. In the human subject the disorder is inoculable at all ages, the only protective influence being a previous successful inoculation, but attempts at inoculation have hitherto always failed in the case of the lower animals. In this the malady differs entirely from tuberculosis. The field for experimental research is therefore very limited. Recently, Van Neissen states that he has succeeded in producing hard sores and gummata in various animals, by inoculating with cultures of the syphilis bacillus he claims to have discovered. This, however, requires corroboration. Various other experimenters have claimed that they have successfully inoculated animals, but it is probable that either matter from soft chancres or tuberculous matter was used. E. Duplan obtained negative results in sixty-eight inoculations, while in the case of two rabbits he probably inoculated tubercle, not syphilis. Ravenel (April 1900) has recorded the failure of his attempt to transmit syphilis to calves.

Modes of infection.—These are direct and mediate infection, and hereditary transmission. In a large number of cases, the disease is contracted during sexual intercourse, by direct contact. Various other modes of direct infection exist, such as kissing, suction of nipple, biting, digital examination by the accoucheur, tattooing in cases where the operator has used his own saliva, circumcision, and vaccination. In mediate infection, the contagion is communicated by means of instruments contaminated with the syphilitic virus, such as drinking-vessels, tooth-instruments, etc. The syphilitic virus can apparently retain its activity in the dried state for many weeks. The virus is contained in the most potent form in the secretions of the initial lesion and of the secondary lesions, condylomata, and mucous patches, as well as in the secretions of similar eruptions in inherited syphilis. The blood, when the disease is active, also contains the virus. Many believe that the secretions from tertiary lesions are inert. The saliva, if the mouth is healthy, the milk, the semen, the sweat, and the tears are also believed to be innocuous. Hereditary transmission may be from the father or the mother. A woman may give birth to a syphilitic child without herself showing symptoms of the disease. In such cases, however, the mother is herself protected, as is shown by the fact that she does not contract syphilis by suckling the child; while an unprotected person, such as a wet nurse, would almost certainly do so. The statement of the immunity of the mother of a syphilitic child is known as Colles's law, having first been enunciated by Abraham Colles, a Dublin surgeon, in 1837. Mention may be made here of the law of Profeta, to the effect that the healthy offspring of syphilitic parents are immune to syphilitic infection. This so-called law rests on much less certain evidence than Colles's law, and must be considered as not proven, if not disproved.

The relation of syphilis to other diseases, such as tubercle and cancer, has received a considerable amount of study. When syphilis is attended with much debility, probably the power of resistance to the

tubercle bacillus is diminished. Some evidence has been collected, showing that syphilitic lesions, especially of the mouth and tongue, may later become cancerous. Aneurysm is believed by many to be etiologically intimately connected with syphilis.

Syphilis contracted at a late period of life is, as a rule, more severe than when acquired early. A second attack may occur, but it is certainly rare, and the number of really authentic cases is few. A second successful inoculation generally produces a milder type of disease, but in some of the genuine recorded cases the second attack has been very severe.

Morbid anatomy. — *Primary sore.* — This consists of a localised tumour of granulation tissue, seated in the cutis vera. In the earliest stages small round cells are clustered round the vessels. There is an infiltration with leucocytes and a proliferation of the connective tissue cells. In the later stages the papillary layer at the margin of the sore becomes swollen, its interstices being distended with fluid and infiltrated with closely-set small round cells, forming an indurated edge to the sore.

The blood vessels in the neighbourhood of the lesion early show changes. The cells of the endothelium swell and proliferate; small round cells infiltrate the walls of the vessels, and the immediately surrounding lymph spaces are crowded with polyhedral cells. The early involvement of the vessels, and the extent to which they are affected, are striking features of the primary sore.

Secondary affections.—*Lymphatic glands.*—The virus is conveyed to the neighbouring glands by means of the lymphatics. The glands show changes similar to those of the original sore, namely, the production of granulation tissue, with little tendency to develop into ordinary connective tissue, and no marked tendency to caseation.

Skin eruptions.—The histological changes in the skin lesions of the secondary period consist of hyperæmia and infiltration with round cells, the former being in excess in the roseolar eruption, the latter in the papular. The infiltrating cells are similar to those which are found in the initial lesion and in gummata, and the degree to which they are present is greater the later the period at which the eruption appears. In the papules it is the superficial layers, the Malpighian layer of the epidermis, and the papillæ which are affected; while in the tubercle the deeper structures are involved as well as the reticular layer of the cutis vera and the subcutaneous tissues. These simple processes may be modified by the invasion of the lesions by pyogenic organisms, by which are produced the pustular and impetiginous forms of eruption.

Later lesions.—Of the later lesions, those which have a characteristic anatomy are certain vascular changes and certain tumour formations called gummata. The vascular changes will be discussed under a separate heading.

Gummata are tumours which at first are composed of granulation tissue, resembling that of the primary lesion. They are mainly made up of small spheroidal cells, but polyhedral and giant cells are occasionally present. Few blood vessels are contained in the new tissues. These tumours may be of miliary size, or as large as an egg or an apple, and sometimes may attain even greater dimensions. They are found in the skin, subcutaneous tissue, bursæ, muscles, bones, periosteum, membranes of the brain, liver, heart, female breast, testicle, etc. In an early stage they have a yellowish or reddish white colour, and though of firm consistence have a somewhat gluey or gelatinous appearance, but they are seldom seen

in this condition. At a later period they appear as greyish white rounded bodies with opaque yellow caseous centres, and somewhat translucent firm fibrous capsules. Caseation is generally widely although unequally diffused, and often starts at a number of separate foci in the interior of the tumour. Fibrous tissue, infiltrated with small round cells, forms at the periphery. The boundary of the mature gumma is not generally sharply defined, but the tumour gradually merges into firm connective tissue, with processes ramifying into the surrounding structures. Gummata in or near the skin or mucous membranes may break down and form ulcers, the walls of which consist of tissue similar to that of the original tumours. In the internal organs they may remain unaltered in the caseous condition for a long time, or they may undergo gradual absorption, leaving no traces of their former presence except fibrous scars, with sometimes calcareous deposits.

Willmot Evans in a recent paper discusses the causes of the localisation of gummata, which he regards as probably the effects of the toxine left behind after the death of the micro-organism; the irritant being a special chemical substance, organic though not organised. He lays down two propositions—first, that gummata tend to appear in structures poorly supplied with blood; and, second, that impairment of nutrition of any tissue is a great incentive to the deposition of gummatous material in it. He points out that the median vertical septum of the tongue is the least vascular part, and here gummata are the most frequent. If a gumma affects a muscle, it occurs in the intermuscular septa or in the sheath. In the joints the capsules, and in the larynx the fibrous perichondrium, are most prone to be attacked. The vascular tissues, such as the lung, spleen, pancreas, and kidney, are rarely attacked. Tubercle, on the other hand, seeks the vascular tissues. The effect of impairment of nutrition is shown by the predisposing influence of injury, or of interference with the circulation. Injury to the tibia is connected with the frequency of nodes on its crest. The exposed position of the knee and its proneness to injury, especially in working women, explains the localisation of a gumma in the skin over it. Excessive use of a joint may determine a gumma in it, as in the case of the right sterno-clavicular joint. The influence of impairment of the circulation is illustrated by the frequency of gummata on the legs when the veins are varicose.

Symptoms.—Acquired syphilis.—Primary stage.—The duration between infection and the first appearance of the primary sore has been variously stated as between ten and ninety days, but commonly is between three and five weeks. Jonathan Hutchinson believes that the usual latent period is longer than is generally taught, and, as a rule, is five weeks; while R. W. Taylor states that the average is between twelve or fifteen and twenty-one days. Seven to fourteen days may elapse after the first appearance of the sore before it acquires diagnostic characters. In eleven patients inoculated by vaccination, the scar showed signs of irritability about five weeks after infection. In cases where the incubation period is reported to have been unusually short, it is probable, as Hutchinson suggests, that the virus was not pure, and that the irritation which first appeared was simply inflammatory, and not specific. In an outbreak of syphilis following the inoculation of the syphilitic virus in the process of tattooing, reported by Surgeon Barker, the incubation period varied between thirteen and eighty-seven days. In three cases, in which tattooing was done on the same day, the periods were twenty-nine, forty-seven, and fifty-nine days respectively.

The primary lesion is, as a rule, a single sore (chancre) with indurated

base. Induration is not present from the beginning, but requires time for its development, and sometimes it is absent throughout.

The most usual site of the primary sore is on the genitals, but it may be found elsewhere, as on the tongue, lip, tonsil, eyelid, nipple, or finger, and indeed any part of the body may be successfully inoculated. An abrasion of the skin or mucous membrane is probably necessary for successful inoculation. Although the sore is usually single, the fact of there being several does not exclude syphilis.

The sore generally begins as a minute, round, reddish, excoriated spot, with smooth polished surface. At first it is not raised, but as it becomes older it becomes more salient, and forms a cup-shaped ulcer with glossy indolent surface and thin, scanty secretion, and a raised, hard, callous border. When the erosion remains superficial, it forms a thin wafer-like or parchment-like mass; when it extends to the subcutaneous tissues, the induration becomes, as a rule, well marked. Various forms of chancre have been described, such as the chancrous erosion, the dry papule, and the ecthymatous chancre, but of these space does not permit a detailed account.

The lymphatic glands in connection with the affected part usually become enlarged and indurated. The enlargement is noticeable within a few days of the appearance of the sore, and the induration follows a little later. The glands, which vary in size from a bean to an almond, are freely movable under the skin, and remain discrete. They are not painful, although they may be slightly tender to pressure, and, as a rule, the patient is quite unconscious of their presence until his attention is drawn to them. The induration of the glands becomes fully developed in one or two weeks, and continues from a few weeks to several months. Suppuration is uncommon, and when it occurs is due to the invasion of the primary sore by pyogenic organisms. Accompanying the induration of the glands there is sometimes also induration and swelling of the lymphatics between the sore and the glands. This induration runs a similar course to that of the glands.

Secondary stage.—Following the appearance of the primary sore, there is a second incubation period, usually lasting about six weeks; its limits being one to three months. The secondary stage of syphilis then sets in, characterised by malaise and fever, together with eruptions on the skin and mucous membranes.

The amount of constitutional disturbance attending the eruptions of the secondary period is subject to great variations. In some cases there may be little or none; in others, especially in women, it may be as marked as in one of the specific fevers. The eruption which is the characteristic of the secondary stage, although very variable in form, is usually coppery or of the colour of raw ham.

The skin.—The secondary syphilides more especially affect the face, particularly the forehead at the margin of the hair, forming the so-called *corona Veneris*, the sides of the nose and the angles of the mouth, the scalp, the abdomen (especially round the umbilicus), the sides of the trunk, the neighbourhood of the anus and genitals, and the palms of the hands and the soles of the feet. They are more marked on the anterior and inner aspect of the limbs than on the posterior and outer. They are, as a rule, symmetrical. Other characteristics are polymorphism, or the occurrence of several varieties of lesion in the same patient at the same time, the absence of itching and pain, and the tendency for the lesions to arrange themselves in crescents or rings.

The eruptions are for the most part chronic, and devoid of inflammatory features. The ordinary secondary eruption takes from two to four weeks for its full development, and some eight weeks for its decline and disappearance. Very transitory and very long-continued eruptions are sometimes observed. The most common as well as the earliest rash to appear is the roseolar or macular. This consists of round spots, generally pink, but varying in shade from a rosy red to a purple colour, and from a quarter to half an inch in diameter. They are usually most marked over the abdomen. At first they fade on pressure, but later they cannot be effaced in this way. The eruption sometimes assumes a papular character, and quite a number of varieties have been described, such as the miliary papular, the lenticular, the small flat, the large flat, and the scaly papular. It may also be of a pustular type, of which an acneiform, a varioliform, an impetiginiform, and an ecthymatiform variety have been described. A rare form of secondary syphilide, described by French writers as the malignant ulcerous, is met with in the so-called malignant form of syphilis to which reference will be made later.

Still another form is the pigmentary syphilide, which may occur alone or with other eruptions. This is most commonly met with in females, especially blondes, up to the age of 30 or 35. It specially affects the lateral surfaces of the neck, but may attack the face and, in particular, the forehead, or the trunk, arms, or legs. It occurs in several forms, and the patches vary in colour from a very light to a very dark brown. After a time the colour fades irregularly, and whitish islets make their appearance. This pigmentary eruption is very indolent, and is but little affected by treatment.

In situations of the body where the skin is usually moist, such as the groins, the vicinity of the anus, the genitals, the axillæ, and the angles of the mouth, the lesions assume a peculiar character, and are termed flat condylomata. These consist of flat roundish and slightly raised discs of a greyish red colour. Sometimes the patches are much raised, when they are called acuminate condylomata.

The affections of mucous membranes.—The eruptions on the mucous membranes consist of erythemata, superficial ulcers, and mucous patches. Erythema of the fauces is common in the early stages, but in itself cannot be considered characteristic. The most typical lesions are mucous patches, and their most characteristic situation is on the tonsils and the anterior pillars of the fauces, but they are also not infrequently present on the uvula, the sides of the tongue, the mucous surfaces of the lips, and the inner surface of the cheeks near the last molar tooth. They have often a greyish white colour, as if the mucous membrane had been pencilled with nitrate of silver. They are not, as a rule, elevated above the surface. With the erythema of the pharynx there is usually dryness of the fauces, together with some discomfort or actual pain on swallowing. When there are mucous patches, soreness of the throat is often a marked feature.

A similar condition to that in the pharynx is not uncommon in the larynx. Hoarseness is a frequent feature of the early secondary stage. This may pass into aphonia. Pain on swallowing may result from the affection of the larynx as well as from that of the pharynx. The pituitary membrane of the nose is also liable to be the seat of erythema, superficial ulceration, and mucous patches. In women the vulva is frequently the seat of mucous patches. The lymphatic glands at this period are often slightly swollen. The swelling is indolent and painless, and the glands

most frequently affected are the anterior and posterior cervical, the occipital, and the supraclavicular.

Fever is a common symptom at the onset of the secondary stage. It seldom makes its appearance earlier than ten days before the rash. It may be slight, which is usual; or it may be intense, which is rare. A mild form of pyrexia is the usual type, the highest temperature not exceeding 101°. In most cases with papular eruptions the fever is mild. In exceptional cases the fever may assume an intermittent or remittent type, the higher temperatures reaching 104° or 105°. Cases have been recorded where febrile temperatures persisted for a long time, until treatment with mercury and iodide of potassium had been adopted.

Anæmia and loss of strength are frequent accompaniments of the secondary period. Anæmia is characterised by pallor, with a slight icteric tinge, and considerable diminution in the number of red blood corpuscles. Weakness or prostration is generally much more marked in females than in males, and sometimes is extreme, with inability to stand or sit up, and very feeble cardiac action.

Headache is a common and troublesome symptom. Following Fournier, we may recognise three varieties of headache: the first troublesome, but not so severe as to prevent the patient from following his or her ordinary occupation; the second resembling migraine; and the third very severe, accompanied by giddiness, tinnitus, and sometimes much mental depression, and totally incapacitating the sufferer from work. The headache may be constant or intermittent; in the first case becoming more severe in the evening, in the second case coming on only in the evening. The patient may suffer from headache for a few days only, or for several months. Insomnia may be present with or without headache, but it is usually in women that it is a marked feature. It is not influenced by ordinary hypnotics, but disappears with antisyphilitic treatment. Neuralgia affecting the fifth cranial or the sciatic nerves, and sometimes the intercostal or the anterior crural nerves, is not uncommon.

The patient frequently, at this stage, loses flesh, and suffers from shifting pains in the bones and joints, or the muscles and fasciæ. These pains, like the headache, may be absent during the day, but coming on towards evening may be very distressing during the night. It is in the larger joints, and in the muscles and fasciæ of the extremities, that the pains most frequently occur.

Synovitis of a peculiar type occasionally occurs. It is usually slow, comparatively painless and intermittent. The amount of effusion may be small or large, and may return again, after disappearing more than once. The skin over the joint is unaffected. The joint may be manipulated without discomfort to the patient. Under treatment the effusion slowly disappears. The joint usually completely recovers, but may be left enlarged and thickened, and subject to recurrent small effusions. Sometimes one meets with a form of joint affection resembling acute articular rheumatism, but differing in its tendency to remain in the parts first attacked. Both large and small joints may be swollen, painful, and tender. The condition may run a protracted course, and be accompanied by pronounced fever. It is intractable to ordinary anti-rheumatic remedies, but gradually yields to antisyphilitic treatment.

The bones also may be affected in the secondary period, especially the skull, the tibiæ, the ribs, the sternum, and the clavicles. In the case of the skull, nodes most frequently appear on the frontal or parietal bones. The subcutaneous surface of the tibia, the upper third of the sternum, and the

inner extremities of the clavicles are particularly liable to be attacked. Pain is sometimes severe, and is usually worse at night. On the whole, periostitis at this stage is slight and transitory.

Affections of the eyes.—Iritis may occur from three to six months after infection, frequently appearing when the eruption is at its height, or just beginning to decline. It is usually symmetrical. Lymph is freely effused, forming nodules of a salmon colour or rusty tint. Ciliary congestion is generally well marked. Relapses are liable to happen, but in these much less lymph is effused, and nodules are rarely seen. Along with iritis, or, instead of it, retinitis may come on. This generally begins at a rather later period than the iritis. There are no subjective symptoms, except dimness of sight. Ophthalmoscopic examination shows haziness of the retina, which appears "as if stained with port wine," and slight swelling of and blurring of the margins of the optic disc, together with small hæmorrhages.

Affections of the ears.—It is not uncommon for the affection of the throat in the secondary stage to be followed, by extension, by catarrh of the Eustachian tube and middle ear. Tinnitus and deafness are the usual results of the chronic aural catarrh. Purulent inflammation of the middle ear, with perforation of the membrane, has not infrequently occurred in the secondary stage. Syphilitic affections of the internal ear, though fortunately rare, are sometimes observed towards the end of the secondary period, or about six months after primary symptoms. The course of these troubles is sometimes remarkably rapid, so that a patient may, in ten days, become absolutely deaf. It is the connective tissue elements which are probably affected, damage occurring to the nerve elements through their infiltration. Such affections require prompt and very active mercurial treatment. When this is adopted early, they usually subside. Sometimes facial paralysis accompanies the deafness.

Alopecia frequently occurs during the secondary stage. It may be slight or almost complete. Two forms of alopecia have been described. One a general thinning, or more or less complete shedding, the other a falling out of the hair in circumscribed patches. The eyebrows, beard, moustaches, and axillary and pubic hair may suffer as well as the scalp. In the patchy form the scalp often assumes a moth-eaten appearance.

The nails also are sometimes affected, those of the feet, as well as those of the hands. The changes in them usually occur during the first two years. The disorder may begin in the nail itself (onychia), or in its vicinity (perionychia). In the latter form the nail is affected secondarily. Various forms of onychia are met with—Onychia sicca, in which the edge of the nail becomes thickened and brittle, and the surface rough and lined with shallow longitudinal fissures; hypertrophic onychia, when thickening is excessive; and a form in which separation of a portion or the whole of the nail occurs. Similarly, there are various types of perionychia —the ulcerative, in which there is ulceration with secretion of pus along the attached nail margins; the non-ulcerative, in which there is much thickening of the attached margin; and a diffuse form, in which necrosis of the nail is apt to occur.

Other disorders of the secondary period which have been occasionally observed are hysteria and analgesia. Fournier observed general analgesia in one hundred cases in three years; and Taylor has frequently met with it both in the male and female. Sometimes it is accompanied by anæsthesia and inability to distinguish heat from cold. Sometimes it is limited to certain parts of the body, especially the extremities of the limbs, and in

women the breasts. Enlargement of the spleen, pleurisy, jaundice, and nephritis are other occasional complications.

Course and duration.—It must be borne in mind that, in an individual case, probably only a few of the symptoms mentioned will be met with. A skin eruption and a sore throat often comprise the whole symptomatology of the secondary period. From six months to a year is the usual time during which secondary symptoms may appear. The actual duration of the secondary symptoms in a case adequately treated may be only a few weeks.

The term malignant syphilis has been applied to certain cases in which the secondary manifestations of syphilis appear with unusual rapidity, and are from the first of a severe type, so as to merit the term malignant syphilis. The constitutional symptoms, such as general cachexia, fever, anæmia, pains, etc., are accompanied with much prostration. The skin lesions are of an ulcerative and pustular type, or various forms of rash follow one another in quick succession, so that the mild and severe eruptions are probably present at the same time. The term malignant syphilis has been also applied to cases of severe tertiary sores, occurring in debilitated or otherwise unhealthy subjects.

Some think that malignancy owes its origin to peculiar virulence of the virus, or to its combination with pyogenic cocci; others suppose that an unusually large amount of the virus has been introduced into the system; while others hold that there must be some peculiar susceptibility in the individual. It has been observed that cases of this so-called malignant type bear mercurial treatment badly, and better success is sometimes obtained by having recourse to iodides. The prognosis, however, is on the whole good.

Tertiary stage.—After the subsidence of the secondary symptoms, a period of more or less immunity generally follows. This is followed in a certain number of cases by lesions differing widely from those of the secondary period. They are slowly evolved and of chronic duration, insidious in their onset, uncertain in their course, and unattended by local or general premonitory symptoms. While the secondary lesions attack the superficial parts, the tertiary invade the deeper, the subdermal, and submucous tissues, the bones, muscles, and viscera. While the secondary are symmetrical, the tertiary show no such arrangement. The secondary as a rule undergo spontaneous retrogression, and seldom if ever recur; while the tertiary exhibit little natural tendency to resolution, and may relapse after treatment again and again. The average time of onset is about the third or fourth year, but tertiary lesions sometimes develop quite early or towards the end of the first year. Haslund gives an estimate, founded on 6364 cases of primary syphilis, that 13 per cent. of the males and 11·7 per cent. of the females have tertiary symptoms. Jonathan Hutchinson, from 2000 private cases, gives a much lower estimate, namely, 7·2 per cent.; and of cases treated by himself throughout, the percentage was much less—little more than 1 per cent. He believes that in cases systematically treated the occurrence of tertiary symptoms is quite the exception. This is supported by the evidence collected by Marschalko, who found, from the study of 673 cases, that tertiary symptoms occurred in only 2·7 per cent. of the cases efficiently treated, as against 23·9 per cent. in the neglected cases.

The skin eruptions of the tertiary period are, as has been pointed out, more deeply situated, and are more scattered, and more irregularly distributed, than the secondary. A number of varieties have been described,

such as the gummatous, the tuberculous, the serpiginous, the rupial, and the bullous. The gummatous syphilide begins in the subcutaneous tissue, and the skin only secondarily becomes affected. The lesions are commonly few, but they may be very numerous. They may lead to extensive ulceration of the skin. They affect specially parts where the skin is soft and connective tissue abundant. Thus, while the neighbourhood of the joints is affected, and the scalp, face, and neck may suffer, the palms and soles escape. Most of the tertiary eruptions leave behind them a coppery stain. The same is observed, although more rarely, after some of the secondary eruptions.

In the tuberculous syphilide there are circumscribed infiltrations, which are deeply seated in the skin, and seldom lead to ulceration. Its course is very chronic, and it frequently relapses. The eruption is attended by no subjective symptoms, and unless it appears early, when it more properly belongs to the secondary period, is limited to one or two parts of the body. Sometimes tuberculous rings or kidney-shaped patches are formed, which grow at their periphery. The surface of such patches frequently becomes warty and uneven. The head and face are not infrequently attacked, and the skin over the sternum, shoulders, inguinal, or gluteal region may also be affected. Over the buttocks the eruption may be covered with scales. This eruption, although very persistent if untreated, generally yields readily to specific treatment.

The serpiginous syphilide, like the tuberculous, is very chronic, and may affect a large surface of the body, creeping along by ulceration at the margin while healing at the centre. It may be deep or superficial. The margin is usually covered with crusts. This form is one of the rarer lesions, and is generally late in making its appearance. It is less tractable than the tuberculous syphilide. Rupia is a syphilide composed of ulcers covered by laminated crusts. It is often attended by fever, and points to a severe type of the disease. It may occur as early as the first year; but as a rule is later, appearing towards the end of the second or about the beginning of the third year. The lesions begin as red spots, and develop into flat pustules, which dry and become covered with greenish brown crusts. The crusts have a diameter of from $\frac{1}{2}$ in. to 2 in. Underneath the crusts are ulcers with greyish red floors and slightly undermined margins. This eruption is always serious and difficult to cure. The larger the lesions, the graver is the prognosis.

The bullous syphilide at first resembles pemphigus; but the effused serum soon becomes altered into pus, which dries into a dark, greenish, adherent crust. This lesion specially affects the forearms and legs. It is always a late eruption, and, if untreated, may pass into a pemphigoid type.

The internal organs.—The tongue, the pharynx, larynx, and the various viscera may be affected with gummata and other lesions, which will be described under separate headings. The blood vessels are very prone to disease, especially the aorta and the cerebral arteries. The lesions affecting them will also be described separately.

Fever, we have mentioned, may occur, not only at the onset of the secondary stage, but sometimes assumes a chronic form. It is important to bear in mind that fever may also complicate visceral syphilis, and in this case the fever may be of long duration, accompanied by malaise and emaciation, unless the nature of the disease is recognised and appropriate treatment adopted.

To complete our account of acquired syphilis, brief mention must here

be made of certain affections of the eyes, subcutaneous tissues, muscles, joints, and bones.

The eyes.—We have seen that retinitis may occur about the same time as iritis. Choroiditis frequently is associated with retinitis, and may occur from six months to two years after infection. It usually affects both eyes, and often gives rise to opacities in the vitreous. The lesions may be limited to the peripheral portions, and cause little damage to sight, or may involve the retina and disc, and progress to almost total blindness. Optic neuritis, when it occurs, is usually secondary to cerebral gummata. The oculomotor nerves are apt to suffer. The third is more commonly affected than the sixth, and the sixth than the fourth. Symmetrical enlargement of the lachrymal glands is one of the rarer affections. The tumours first produce ptosis, and sometimes puffiness and slight redness of the eyelids, and later are apt to involve the nerves and muscles of the eyeballs, thus limiting movement and producing anæsthesia of forehead and scalp. Perfect recovery follows efficient treatment.

The subcutaneous tissues.—These are frequently the seat of gummata. Where adipose or cellular tissue is abundant, such tumours may long exist without the skin becoming involved. Gummata of the scalp seldom form isolated tumours. The integument as a whole becomes thickened and adherent to the bone, which is usually also involved. On the face, however, there may be movable subcutaneous tumours as well as diffuse infiltrations. The latter may lead to serious distortion. Gummata are not infrequent in the female breasts. They form painless tumours of slow growth, and of moderate hardness. The axillary glands remain unaffected. Gummata of the gluteal regions and of the thighs sometimes attain a remarkable size. Subcutaneous gummata may be seated over nerves, and give rise to severe pain. In the lower extremities, what have been called cellular nodes are not uncommon, usually occurring near the knee, and more often in women than in men. The node ultimately ulcerates, and shows a core which has been likened in appearance to soaked washleather. The subcutaneous bursæ are not infrequently attacked, especially the bursæ patellæ. Gummata form in them insidiously without pain, and ulceration occurs in the same way as in the case of the cellular node. In these cases there is sometimes a history of traumatism.

The muscles.—Two forms of affection of muscles have been described. They are among the more remote sequelæ of syphilis, and are decidedly rare. A form of myositis has been observed, tending to more or less permanent contraction of the muscle. Between the interstices of the muscular tissue there is a development of connective tissue, which contracts and ultimately destroys the muscle fibres. Such an affection has been most frequently observed in the case of the biceps. Contraction gradually takes place, and the only change observed is an apparent diminution in the length of the muscle. The limb becomes flexed, and cannot be completely extended. In some cases there is no pain, in others there is a dull aching. The affection tends to be progressive, unless suitably treated, but it may be recovered from spontaneously.

Gummata develop slowly in muscles, without pain. There is usually very considerable and well-defined induration. Sometimes a large mass of muscle becomes involved. The substance of the tongue is more frequently affected than other muscles. The sterno-mastoid, the masseter, the supra- and infra-spinatus, the gastrocnemius, and the rectus femoris, are specially mentioned by Jonathan Hutchinson as liable to be affected. Muscular

gummata are of various shapes and sizes, and may be flat, fusiform, globular, or irregular. They are frequently situated near the ends of muscles. Exceptionally they break down and form deep ulcers. The tendons, especially near their insertions and in the thicker portions, and the tendinous sheaths may also be affected.

The joints.—The joints, which as we have seen, may be affected in the secondary stage, are very rarely involved in the later stages. It is usually the larger joints, especially the knees, which suffer. The type of affection is subacute. The joints become swollen, from thickening of the ligaments and the fibrous and loose connective tissue surrounding the capsule, and from gummatous infiltration of these tissues or of the cartilages or epiphyses. Effusion usually comes on slowly, and pain may or may not be a marked symptom. These joint affections yield less readily to treatment than those of the earlier period, and it is very important that vigorous antisyphilitic measures should be employed before there is much thickening and consequent impairment of movement. In several instances collected by Jonathan Hutchinson, jun., the joint lesion was the only existing symptom of late syphilis.

The bones.—Affections of the periosteum and bone are among the most frequent of the tertiary lesions of syphilis. Periosteal nodes seldom occur earlier than two years from infection, and often are much later. The superficial bones, such as the tibiæ, the ulnæ, the clavicles, the sternum, and the calvaria, are most liable, probably on account of their exposed situation. The palate bones, the bones of the nose, and the alveolar processes of the maxillæ, are also frequently affected.

Nodes are ill-defined doughy tumours, adherent to the bone but not to the skin. They consist of inflammatory tissue in the substance of the periosteum or between it and the surface of the bone. They are usually the seat of severe nocturnal pains. Sometimes the affected bone becomes greatly thickened and more dense, as, for instance, in the case of the calvaria. Nodes may develop on the internal aspect of the skull as well as on the external, and various cerebral symptoms may ensue. Sometimes the node becomes indurated, and eburnated bony tissue develops, forming an exostosis. On the other hand, suppuration may take place, with the formation of a periosteal abscess, or an ulcer exposing the bone, portions of which may separate by exfoliation.

Hereditary syphilis.—The symptoms of hereditary syphilis consist in the presence of certain eruptions on the skin, together with a form of nasal catarrh, commonly first known as snuffles. These symptoms usually appear about the third week. Exceptionally they are present when the child is born. In other cases they may not appear till about the twelfth week.

The *rashes*, usually copious and symmetrical, are as variable as in acquired syphilis, but the commoner are erythematous, eczematous, or papular. The erythema is characterised by its abrupt margin and its red or coppery tint. Dry, scaly, vesicular, pustular, or bullous eruptions may also be met with. The rash is generally well marked on the nates, the thighs, and the genitals, and condylomata may also be observed about these parts. Mucous patches are frequently present on the mucous membrane of the mouth, especially about the angles of the lips and the mucous surface of the cheeks, the fauces, tonsils, and the sides and dorsum of the tongue. The secretion from these patches is abundant, and is highly infective.

Snuffles results from an inflammatory condition of the nasal mucous membrane. It is not only one of the earliest symptoms, but also one of the

most constant. There is swelling of the mucous membrane, together with a serous discharge, which may interfere with respiration, especially during sleep and suckling. The obstacle to the breathing gives rise to the characteristic snuffling sound. · The discharge, at first thin, presently becomes thick, and dries into crusts. Sometimes it is blood-stained, and it may be offensive. In mild cases, the affection is nothing more than an erythema; but in the severer cases there is ulceration of the mucous membrane, the bones become affected, and the destruction of bone may be followed by serious deformity.

Although the victims of hereditary syphilis may be born healthy-looking, it is soon apparent that they do not thrive. They waste, lose colour, and acquire a wizened appearance. The skin of the face is sallow, and tightly stretched over the bones, while that of the body is loose and wrinkled. The little patients look like little old men or women. The bones are often affected early. The most characteristic lesions are swellings at the junction of epiphyses and shafts, forming collars or rings. The bones most usually affected are those of the forearms, arms, legs, and thighs, together with the clavicles, sternum, and ribs. The distal extremity is more likely to be the seat of disease than the proximal, but the sternal end of the clavicle is a common situation. The joints may be secondarily affected, and suppuration may occur from this cause as well as independently. Mention must also be made of a very characteristic joint affection which occurs fairly frequently during childhood or at puberty, and takes the form of a chronic effusion into one or more joints, especially the knees. It is symmetrical, and as a rule almost painless. It may subside spontaneously after a month or two, or may persist for a year or more. It is usually observed in association with interstitial keratitis, which it more frequently follows than precedes. Antisyphilitic treatment is usually quite successful in removing all traces of the malady. Periostitis is usually a late disorder. Dactylitis, especially of the proximal phalanges, is a very characteristic lesion. In this affection the bones may be very greatly enlarged, and the overlying tissues may swell and suppurate. Onychia is less common than in acquired syphilis, but is met with in two forms— ulcerative and non-ulcerative.

Gastric and intestinal disorders are not infrequent, but are probably not of specific origin. The spleen is frequently enlarged—in half of the cases, according to Gee, while in one-fourth the hypertrophy is excessive. Pericellular cirrhosis, with or without gummata, also occurs. Affections of the liver are further discussed under a separate heading. The pancreas sometimes undergoes degeneration. It becomes abnormally firm and of a glistening white colour, due to great increase of the interstitial connective tissue.

General adenitis does not occur in the inherited form. When the cervical glands are affected, this is secondary to lesions of the mouth and throat. Occasionally abscesses or a diffuse suppurative inflammation in the substance of the thymus have been observed.

The larynx is occasionally affected, but seldom in children younger than seven years. Ulceration of the epiglottis, with exposure of the cartilage, is the usual form; but there may be general ulceration of the upper part of the larynx, with resulting stenosis. The lungs may be attacked with a form of broncho-pneumonia and with gummata, but specific lesions are decidedly uncommon, as they are in the acquired form.

Lesions of the kidneys are sometimes observed, due to proliferation of

the connective tissue and fatty degeneration of the epithelium. The suprarenals may be enlarged. Affections of the testicles are rarer than in acquired syphilis. Orchitis may occur between the ages of 3 and 12, but may be met with later.

Iritis is one of the rarer early manifestations of hereditary syphilis. It usually occurs about the age of 5 months. It may or may not be symmetrical. Subjective symptoms are slight. The effusion of lymph is great, and there is danger of occlusion of the pupil. It responds well to mercurial treatment, which may procure the complete absorption of the effused lymph.

Although, as a rule, the earlier manifestations of hereditary syphilis tend to spontaneous cure, death is not an uncommon result.

During the later period the patient may be free from symptoms. Growth and general development may advance very slowly. While the infant looks old, the adolescent appears infantile. The youth of 18 or 20 may well pass for 12. According to Jonathan Hutchinson, however, this is a very untrustworthy indication, and he thinks that in most cases no retardation of general growth is observable. He considers a pale complexion as the rule. The physiognomy is peculiar : the forehead may be prominent, with protuberant frontal eminences, the bridge of the nose sunken, and the upper incisor teeth prematurely lost. The rash of infantile syphilis, once it has disappeared, seldom returns, but it leaves its traces. There are often pit marks and linear scars near the angles of the mouth.

The permanent teeth.—All the incisor teeth may be dwarfed and deformed, but it is the upper central incisors in which the changes are most marked. The typical tooth is short and narrow, and there is atrophy of its middle part, causing a single broad vertical notch in the edge, from which sometimes a shallow furrow passes upwards on both anterior and posterior surfaces. The tooth is narrower at the cutting edge than at the root, and from this circumstance is often described as peg-like. The affected teeth sometimes converge and sometimes diverge, or they may stand widely apart. The malformation is not shown in the milk teeth. Only the permanent teeth are affected. Jonathan Hutchinson first described these changes. He says that he has never yet seen such teeth excepting in patients who are the subjects of inherited syphilis; but that in the majority of cases, however, the condition of the teeth is sufficient only to excite suspicion and not to decide the question of this disease. In a few rare cases, only one of the central incisors may be deformed.

Syphilitic keratitis.—Both eyes are, as a rule, simultaneously affected. The cornea becomes generally opaque from the effusion of lymph into its substance. Ciliary congestion is an early symptom. At first cloudiness appears in patches, the surface looks steamy, and later the whole cornea becomes hazy, presenting a ground-glass appearance. The tint may vary from a dull grey to a red salmon colour. There is usually considerable photophobia. In many cases iritis occurs, with the formation of posterior synechiæ. While the condition persists, the patient is almost completely blind. After lasting several months, the opacity clears away, but generally leaves traces, slight clouds remaining here and there in the cornea, together with some duskiness of the sclerotic in the ciliary region. Keratitis usually occurs between 6 and the age of puberty, but it may occur as early as 2 or 3 years, and it has been observed as late as 35.

In forming an opinion as to whether a patient has been affected by inherited syphilis, examination of the eyes is often most helpful. They

should be examined both by direct illumination with the help of a lens, and by the ophthalmoscope. Tags resulting from past iritis, and nebulæ on the corneæ, may be of great assistance in completing the evidence in a doubtful case.

Deafness.—It has been estimated that the ears are affected in 10 per cent. of all children with inherited syphilis. The middle or internal ear may be disordered, and total deafness may be produced. The disturbance of hearing may first occur at puberty.

Gummata may occur in various organs at a late period in hereditary syphilis. In the account of visceral syphilis, further mention will be made of these lesions.

Visceral syphilis.—Digestive system.— *The tongue.*—Superficial affections are common in the secondary stage. There may be hyperæmia, accompanied by excoriated or smooth, round, or oval patches. Mucous patches are frequent along the sides and tip. Fissures may appear over the dorsum or sides. In later syphilis we meet with two main forms—sclerosis and gummata. Sclerosis may be superficial or deep, but in either case it affects the upper surface, especially the vicinity of the middle line. In superficial sclerosis, the lesion is limited to the mucous membrane, and there is a lamellated induration, which may be circumscribed or diffuse. In deep sclerosis, the muscular tissue as well as the mucous membrane is involved. The tongue is increased in size. Its surface is lobulated and furrowed, in consequence of the contraction of the newly-formed connective tissue. The mucous membrane itself may be pale and smooth. Gummata may form either superficially, or in the substance of the muscle. Ulcers are usually multiple, are always on the upper surface, and are frequently central, or situated at the sides or tip. They are not usually painful, and the glands, as a rule, are not involved.

The pharynx. — The affections of the secondary stage have been previously alluded to. Tertiary lesions of the soft palate are not uncommon. Gummata may form within its substance, and before the patient makes any complaint perforation may have occurred. Sometimes the soft palate and uvula have been already destroyed by ulceration when the patient first seeks advice. Absence of pain is a characteristic of these lesions, and accounts for the fact that they are allowed to make such ravages. Gummata may also form in the pharyngeal wall, giving rise first to prominent roundish swellings covered by congested mucous membrane, and later to deep crater-like ulcers with raised margins and floors covered with yellow pus. Considerable deformity may result from such lesions. Ulceration is followed by cicatricial contraction. The remains of the soft palate may become adherent to the pharyngeal wall, and only a very narrow opening may be left leading to the naso-pharynx.

The salivary glands are rarely affected. The parotid occasionally becomes swollen during the period of active symptoms. Small tumours, probably gummata, occasionally appear in the sublingual gland.

The œsophagus.—Syphilis of the œsophagus is extremely rare, and, as far as is known, only occurs in the tertiary period. Only twelve undoubted cases had been recorded up to 1890. These have been of the nature of gummatous ulceration, leading to stricture.

The stomach and intestines. — Syphilis of the stomach is likewise extremely rare, and only fourteen of the cases recorded up to 1898 have been properly verified; of these cases five were of the inherited and nine of the acquired form. The lesions met with have been gummata, origin-

ating in the submucous tissue, and chronic ulcers. The gummata form flat plaque-like tumours, and are more commonly multiple than single. The ulcers are more often single than multiple. Syphilitic ulcers in parts of the intestinal tract, other than the rectum, have been recorded, but are very rare.

The rectum.—The rectum is not very infrequently the seat of syphilis in women, but hardly ever in men. Taylor describes three forms of rectal syphilis—(*a*) The extension of indurating œdema from the vulva or vagina to the rectum, leading to the production of more or less complete rings of connective tissue, situated either between the two sphincters, or about 1, 2, or 3 in. above the internal one. This occurs either early or late in the disease, but usually in the secondary or early tertiary stage. (*b*) Gummatous infiltration producing patches of thickened mucous membrane, some little distance from the anus. (*c*) The development of a form of infiltration with the production of new connective tissue, without congestion or exudative products. An annular stricture may in this way be produced long after the activity of the disease has ceased. The process is one of very slow progress.

Liver.—The liver is probably more frequently attacked by syphilis than any other internal organ. Three forms have been described— perihepatitis, gummatous hepatitis, and diffuse hepatitis. It would be impossible to conclude that perihepatitis was syphilitic, unless it were associated with other lesions, such as the fibrous scars left by gummata or gummata themselves. At the same time its association with other lesions does not prove it to be itself syphilitic.

Gummatous hepatitis is the most characteristic form. Gummata are found in the liver in both congenital and acquired syphilis. They are more common in cases of delayed congenital syphilis than in young children, and in the acquired form they rarely occur during the first two years of the disease. As observed at post-mortem examination, the gummata are found surrounded by cicatricial fibrous tissue, producing scarring of the surface. The gumma is caseous at its centre, while sometimes the vessels at its periphery are dilated. The centre varies in consistence from that of cream cheese to a gristle-like toughness, or it may be of almost bony hardness from calcareous deposit. Fibrous bands may extend in various directions from the fibrous periphery of the gumma. The gummata vary in size and number in different cases. Sometimes they may produce great puckering and deformity of the organ.

The diffuse form of syphilitic hepatitis is most commonly met with in congenital syphilis, and generally in quite young children, although I have recorded a case occurring at as late an age as 15. The organ is large, heavy, tough, and of normal shape, and great increase in connective tissue is to be made out. This not only surrounds groups of lobules, but is abundantly present in the lobules themselves, passing between individual cells, or encircling groups of small cells. Miliary gummata, consisting of small-celled infiltrations, are frequently to be met with. The liver cells, from the compression to which they are exposed, here and there are atrophied or fatty. Larger gummata are not frequent in this form of hepatitis, although they do occur.

Acquired syphilis of the liver is more frequently observed in men than in women. It is most common from three to seven years after infection. Rarely it occurs during the first year. It may occur as late as twenty-five years after infection. In some of the cases there is a distinct history of trauma.

In the gummatous form the liver will probably be palpably enlarged, and a hard nodular mass may be felt in the epigastric region or right hypochondrium. Apart from the presence of the tumour, the patient may have no symptoms, but jaundice and fever may be present. In such cases a history of syphilis is a most important aid to diagnosis. Confirmatory evidence may be obtained by examination of the eyes, and the finding of opacities of the corneæ, signs of old iritis or choroidal changes, or by the presence of scars on the shins, fauces, or elsewhere. Fever is by no means a constant symptom. It was present in a well-marked case of syphilitic tumour of the liver, in a boy under my observation, and disappeared as soon as treatment with iodide of potassium was started. Pain is not an infrequent symptom, but it is seldom severe except where there is perihepatitis. In diffuse syphilitic hepatitis, jaundice is a common symptom. Ascites may or may not be present. The spleen is not uncommonly enlarged as well as the liver. When amyloid disease coexists, there may be albuminuria. A mild transitory form of jaundice, coming on suddenly and lasting a few weeks, is sometimes observed during the secondary period of syphilis, or in the course of the first year. It is not usually accompanied by loss of appetite and disordered digestion, as in ordinary catarrhal jaundice. It is readily influenced by antisyphilitic treatment. A severe form of jaundice, the pathology of which is obscure, has been described as a late symptom in the course of syphilis. The jaundice is intense and persistent, and is accompanied by cachexia, headache, and neuralgia.

The pancreas.—Syphilitic disease of the pancreas is very rare in acquired syphilis, and then generally takes the form of gummatous infiltration. It is more common in hereditary syphilis, and not a few cases have been observed in infants and new-born children. The pancreas may be attacked as early as the fifth month of gestation. Gummata are rare, the disease usually taking the form of a diffuse interstitial pancreatitis. The organ is not much enlarged, but is increased in weight and is always abnormally firm in consistence. In typical cases it may be as tough as cartilage. The disease as a rule is more advanced towards the head.

Lymphatic system.—*The lymphatic glands.*—It has been mentioned that there is a general enlargement of the subcutaneous lymphatic glands in the secondary stage of syphilis, in addition to the early enlargement of the glands which are in immediate anatomical relation to the primary lesion. The enlargement is most obvious in the glands which are most easily accessible, such as the anterior and posterior cervical, the supraclavicular, the posterior auricular, the occipital, the epitrochlear, and the axillary. The superficial lymphatic glands may again be affected in late syphilis, but are not enlarged secondarily to lesions of skin, mucous membranes, or muscles, an important point in establishing a diagnosis between syphilis and cancer. The deep lymphatic glands may be affected in tertiary syphilis. Thus the glands in anatomical relation, with a tertiary lesion of one of the internal organs, may become indolently enlarged. Independently of any local lesion, the prevertebral, the lumbar, the iliac, and the deep inguinal glands may be enlarged, and be either soft or indurated.

The spleen.—Swelling of the spleen is not uncommon during the secondary period. According to Quinquand and Nicolle, enlargement of this organ is one of the early symptoms of general infection, and may be noticed soon after the appearance of the chancre before either skin or throat

troubles have occurred. At later stages the spleen may be affected, either with an interstitial infiltration or with gummata. Both of these are decidedly rare, and are chiefly met with in congenital cases. In the interstitial form, the organ is permeated by bands of connective tissue, usually following the course of the blood vessels. Gummata may be solitary or multiple, deeply seated or at the surface, and, while ordinarily small, varying in size from a hempseed to a walnut, are sometimes very large, forming a considerable portion of a much enlarged spleen. When recent they are of a reddish grey colour, somewhat denser and tougher than the normal spleen substance. The older lesions, like those in the liver, are embedded in scar-like cicatricial tissue. With either form the capsule is usually thickened, and this may also occur independently. Lardaceous degeneration may be met with both in acquired and congenital syphilis.

The **vascular system.**—*The heart.*—Syphilitic affections of the heart may be classified as follows—Gummata; fibroid induration; amyloid degeneration; infarctions caused by endarteritis obliterans.

Gummata are usually met with in the wall of the left ventricle, or more rarely in that of the right. They are commonly single, although occasionally multiple. Their size ordinarily varies between a bean and a hazel-nut, but they have been met with as large as a hen's egg. It is seldom that an opportunity occurs for seeing them in the recent stage. Loomis observed one of a reddish or reddish grey colour and homogeneous structure, which was co-existent with a well-marked gumma of the liver. The old gummata are of a grey or greyish yellowish colour, of firm consistency and of homogeneous structure. The centre is lighter in colour, of cheesy appearance, but firm. The tumours are not circumscribed, but blend insensibly with the surrounding muscle, the gummatous tissue being continued between the fibres. The peripheral part is composed of small cells, but the caseous centre distinguishes the tumour from sarcoma. It is not always easy to differentiate gummata of the heart from tuberculous lesions. The absence of bacilli and the presence of syphilitic lesions elsewhere are the chief points in favour of syphilis.

The fibroid induration produced by syphilis closely resembles ordinary fibroid disease of the heart; in fact, it is only its association with other evidences of syphilis, such as gummata of other organs, which points to its syphilitic character. The fibroid patches are found most commonly in the wall of the left ventricle, near the apex or at the base near the aorta. The heart, as a rule, is hypertrophied, and the cavities are dilated. The fibrosis may be limited to a well-defined area in the substance of the muscle, from which the muscle fibres have quite disappeared. There may be diffuse irregular patches of new fibrous tissue, with thickening of the overlying pericardium and changes in the arteries (endarteritis obliterans). The fibrosis may represent gummata which have undergone absorption.

Amyloid degeneration in the heart is very rare, but a few cases have been recorded. Endarteritis obliterans usually occurs in association with the changes of fibrous character. The symptoms met with in cases of syphilitic disease of the heart have been irregular and rapid cardiac action, palpitation, dyspnœa, præcordial pain or uneasiness, angina pectoris, and attacks of syncope or epilepsy. It is obvious that there are none of these symptoms which may not accompany other forms of cardiac disease, but the occurrence of such symptoms in early adult life without definite cause,

such as valvular disease, rheumatism, or excess in tobacco, should suggest a suspicion of syphilis. Syphilitic disease of the left side of the heart may be characterised by gradually increasing feebleness without dilatation; and similar disease on the right side, by persistent dyspnœa. Hypertrophy of the heart without increased power, in the absence of obvious cause, suggests syphilis. Sudden death is not infrequent. This occurred in eight out of fourteen cases collected by Duckworth; and out of sixty-three cases collected by Mraček, it occurred in twenty-one. Other observers have noted sudden death in half of the cases. Rupture of the heart has occasionally occurred. At other times death occurs with symptoms of slowly increasing cardiac failure, and the formation of cardiac thrombus.

If specific treatment is started early, the prognosis is good; but when the disease is well advanced, no improvement from iodide of potassium can be looked for.

The arteries.—Syphilitic arteritis may occur during the first year of acquired syphilis, but is more common during the tertiary period, at any time up to twenty years after the primary sore. It also may result from inherited syphilis, then occurring before the tenth year. It most usually affects the cerebral arteries, especially the basilar, the middle cerebral, the vertebral, the internal carotid, and the posterior cerebral. Often several branches are affected simultaneously. The vessels may be diseased for from $\frac{1}{2}$ to 1 in. of their length, and generally in the whole of their circumference. Although the lesions resemble those of atheroma, they differ in their seat, and in the period of life at which they occur, as well as in their course, which is fairly rapid. In this lesion it is the inner coat which is chiefly affected. The intima becomes greatly thickened, and generally asymmetrically so. The space between the endothelium and the membrana fenestrata becomes occupied by a finely granular substance, a kind of ill-developed connective tissue, containing a few nuclei and nucleated spindle-shaped and stellate cells. The growth may be fibroid, hyaloid-looking, or caseous, according to the stage of the disease. The endothelium becomes thickened, and the lumen of the vessel is gradually encroached on. Small round cells may also make their appearance in the middle and outer coats. Thrombosis gradually occurs, as the lumen of the vessel becomes more contracted.

Another variety has been described as syphilitic periarteritis. In this the main lesion is situated in the tunica adventitia, and is of a gummatous nature. Growths of a considerable size may form in this situation.

Respiratory system. — *The nose.* — Secondary affections of the pituitary membrane are relatively not very common. They consist of hyperæmia, superficial ulcers, mucous patches, and redundant adenoid tissue, and give rise to symptoms resembling a troublesome catarrh. Tertiary perforation of the septum is not infrequent. When the vomer is affected, the bridge of the nose may fall in, producing a characteristic flattening, while the tip becomes depressed when the cartilage is destroyed. In tertiary lesions the discharge is generally abundant, and very offensive when the bone is carious.

Larynx.—Statistics show that the larynx is affected in the course of syphilis in from 3 to 4 per cent. of all the cases. The lesions are for the most part slight, and are of a serious nature in not more than a ninth or tenth part of these cases.

Simple catarrh of the larynx has already been referred to as not uncommon during the early secondary period. It may recur or come on

for the first time later. There is nothing characteristic about the appearance of the larynx, which simply shows hyperæmia and congestion. Mucous patches, condylomata, and limited superficial ulcerations may also occur during the secondary period, but are much less common than simple catarrh. In tertiary syphilis, diffuse infiltration, gummata, perichondritis, and destructive ulceration, with ensuing cicatricial contraction, are the principal lesions met with. Gummata and perichondritis of the epiglottis and arytenoids are not uncommon. The perichondritis results in caries and necrosis of the cartilage, with subsequent separation of the diseased part. The epiglottis, or the arytenoids, may be wholly destroyed. Ulcers are usually large, deep, sharply limited, and have a worm-eaten floor. They are often unilateral and solitary. Frequently there is a marked absence of pain, although there may be a considerable amount of dysphagia when the epiglottis is much affected. Syphilitic ulceration usually progresses rapidly. The lesions are surrounded by a zone of congestion and œdema. The upper surface of the epiglottis is more frequently affected than the lower. The ary-epiglottic folds, the ventricular bands, and the vocal cords are not uncommon seats of ulceration. Paralysis of the vocal cords may result either from local syphilitic disease, or from lesions involving the nerves or their nuclei. Stenosis of the glottis sometimes follows extensive ulceration.

The diagnosis has to be made from tubercle and new growth. The hyperæmic appearance, the rapidity of progress, and the extent and destructive character of the ulceration, probably limited to one side, help to distinguish it from tubercle. There may be great difficulty in differentiating syphilis of the larynx from carcinoma. Ulceration proceeds more rapidly in syphilis than in carcinoma, and in the latter the growth is often nodular. Pain, fœtor, and hæmorrhage are much more frequent in carcinoma than in syphilis. Enlargement of glands is in favour of carcinoma.

The prognosis as regards life is not unfavourable when treatment is efficiently carried out. The most serious result is usually stenosis, for which tracheotomy may be necessary, and there may be permanent alteration or even loss of voice. Rarely, acute œdema or hæmorrhage may carry the patient off.

Local treatment is rarely called for. Insufflations or antiseptic spraying may be necessary in the case of necrosing perichondritis, or of foul ulceration. Stenosis may require intubation or tracheotomy. Dilatation by Schrötter's bougies or O'Dwyer's tubes, as a rule, affords only temporary relief. General treatment must be carried out on the usual lines.

Syphilis of the trachea, though a rare affection, is of considerable importance. It occurs during the tertiary period, and has usually been met with in subjects between the ages of 25 and 50. Persons exposed to irritating dust appear specially liable. It occasionally occurs in congenital as well as in acquired syphilis.

Tracheal syphilis usually occurs in the form of gummatous infiltration in the submucous tissue, and may be unassociated with lesions elsewhere in the respiratory tract. Its most usual seat is the anterior surface of the lower portion of the trachea, just above the bifurcation. The gummata soften and ulcerate. Multiple perichondritis is readily set up, and detached portions of cartilage may project into the trachea, and may be separated and expectorated. Ulceration is usually followed by great cicatricial contraction, and the calibre of the trachea may be reduced to

that of a crow-quill. There may be dilatation above and below the annular stricture, but the stenosis involves generally a considerable portion and sometimes the whole length of the tube. While the ulcers, as a rule, heal, they may perforate into the œsophagus, superior vena cava, aorta, or other neighbouring part. Adhesions to the œsophagus may interfere with the upward movements in deglutition.

The main symptoms are inspiratory stridor and dyspnœa. The dyspnœa will vary in proportion to the degree of stenosis. Importance was at one time attached to absence of laryngeal excursions as a point of importance in the diagnosis of tracheal stenosis, but later experience has shown that this cannot be depended on. The head is often bent forward, instead of being thrown back, as in laryngeal dyspnœa. Cough and expectoration frequently precede the dyspnœa. There may be attacks of paroxysmal dyspnœa, from the accumulation of secretion below the point of stricture; and the diagnosis between aneurysm compressing the trachea and syphilitic stenosis may be by no means easy. The voice is often hoarse or croupy, or it may be simply weak.

Syphilis of the bronchi.—A few cases have been recorded where one or both main bronchi have been affected with syphilitic stenosis without the trachea being involved, but it is more common for the disease in the bronchi to be secondary to, or accompanied by, disease in the trachea. Rolleston and Ogle, who could collect only ten cases in literature (*Clin. Soc. Trans.*, 1899), consider that when both bronchi are affected, the stenosis is more probably part of a diffuse syphilitic change, often also involving the lungs, and of the nature of a peribronchitic fibrosis, than a primary syphilitic lesion, sharply limited to the main bronchi, and due to the previous ulceration of gummata, while when one bronchus is affected the stenosis is probably the result of the cicatrisation of an ulcer.

The symptoms of stenosis of both bronchi will be similar to those of stenosis of the trachea. The acute onset of grave symptoms after a long period of latency may be the result, as Rolleston and Ogle suggest, of retained secretion, increased in amount from an accidental bronchial catarrh.

Syphilis of the lungs is a very rare condition, much more so than the similar affection of the trachea. It is seldom diagnosed during life. More cases are met with in men than in women. It is apparently not more common in those affected with chronic pulmonary lesions than in others, and it is not often found simultaneously with tuberculosis.

There are two forms in which syphilis is met with in the lungs in cases of acquired syphilis. These are gummata and disseminated fibrosis or induration. The two forms are frequently combined. Mention must also be made of a form of consolidation found in the lungs of newly-born syphilitic children. It is seldom that an opportunity arises of seeing gummata in early stages. Fibrosis is essentially an old or chronic lesion.

Gummata are frequently combined with broncho-pneumonia. They are usually few in number, often solitary, and rarely are there more than six or eight. They have a round or ovoid form, and vary in size from a pin's head to a walnut or Tangerine orange. They may be superficial or deeply situated, and, as a rule, affect only one lung. They are not usual at the apex, but more commonly are situated about the middle or lower part of the upper lobe or near the hilus. They have a greyish white colour, and are of firm consistence externally, although tending to soften at the centre. While the outer part consists of fibrous tissue, the centre probably is com-

posed of yellowish detritus, which gradually discharges into the bronchi. Thus cavities as large as the original gummata may arise, surrounded by firm fibrous walls. The cavities may persist or become gradually occluded from contraction of their walls. The centre may be the seat of calcareous deposit.

In distinguishing gummata from tubercles, the following points should be considered—their seat, number, colour (which is white or yellow and never translucent), and consistence, which is always harder and more resistant than that of tubercle.

Syphilitic fibrosis often commences round the medium-sized bronchi and the bronchial arteries near the hilum, whence it radiates into the rest of the lung, gradually invading the alveoli. The indurations are formed by connective tissue of the embryonic type, which replaces the pulmonary parenchyma. Bronchiectasis may follow, or the bronchi may be more or less obliterated. This form of lesion has no precise seat. It may occur indifferently at the middle or at the base, but rarely affects the apex. Ordinarily it is bilateral, and it may be circumscribed or diffuse. The pleura usually takes part in the process, the two layers becoming adherent and thickened. Syphilitic fibrosis is difficult to distinguish from tuberculous, except when it is associated with gummata or unmistakable syphilitic lesions elsewhere.

A remarkable condition of consolidation has been observed in the lungs of newly-born children infected with syphilis. The lungs are distended so as to fill the thoracic cavity completely, and are marked with the impressions of the ribs. The pleuræ as a rule are unaffected. The whole of both lungs may be affected, or the morbid change may be partial. The consolidated tissue is four or five times heavier than normal. On section, it appears white with a shade of yellow, and the cut surface is smooth and opaque.

It is usually dense and resistant, but may be friable. The whiteness of the structure results from its bloodlessness, neither blood nor smaller blood vessels being present, except in the interlobular tissue. The bronchial glands are enlarged and of a greyish caseous appearance. According to Wagner, the consolidation results from a thickening of the walls of the alveoli whereby their cavities are gradually obliterated. The epithelium is but little affected. The thickened walls, when examined microscopically, show the presence of an imperfectly fibrillated tissue, with an almost complete obliteration of the capillaries and small vessels; the interlobular tissue may be normal. When the consolidation is partial, there may be isolated patches resembling gummata. Similar changes have been recorded in the lungs of adults.

There is nothing pathognomonic about the symptoms of syphilis of the lungs. In the early stages the symptoms are usually those of laryngeal and bronchial catarrh with some alterations of the voice, cough, and shortness of breath. At a later period cough is more troublesome, and dyspnœa becomes more marked. Expectoration at first is usually scanty and mucoid, but later is probably purulent, and may be offensive. The absence of tubercle bacilli in the sputum is an important point, but fragments of pulmonary tissue may be present. Hæmoptysis, slight in some cases, profuse in others, is not infrequent. The dyspnœa may be paroxysmal, coming on in attacks resembling spasmodic asthma, and associated with pain in the side. Attacks of this nature, as has been mentioned, may also be met with when the trachea alone is involved. The temperature is not usually raised, but fever has been a feature of some of the recorded cases.

Sometimes the patient keeps in good general condition, but this cannot be said to be the rule. Emaciation, anæmia, and marasmus are frequently observed. The physical signs met with are those of consolidation or of excavation, and these are probably observed in an unusual situation for a tuberculous lesion. Although the middle portions of the lungs are the most likely situations in which to find abnormal physical signs, the apices and bases are also sometimes affected.

The occurrence of symptoms such as have been mentioned in a patient with a history of syphilis, or with syphilitic lesions or traces of them in other parts of the body, would probably rightly lead to a diagnosis of syphilitic disease of lung. We may suspect syphilis, in the absence of confirmatory evidence of the disease, in cases where tuberculosis can be excluded and malignant disease is unlikely. A trial of antisyphilitic treatment is always necessary to complete the diagnosis. It should be remembered that syphilis and tubercle have occasionally been met with in the same lung.

Of sixty-two cases collected by Carlier, thirty-eight died and twenty were cured. The prognosis is good, if energetic antisyphilitic treatment is adopted, unless the pulmonary lesions are associated with grave disease of the other viscera. The occurrence of albuminuria appears to render the prognosis more unfavourable. Out of forty-four fatal cases collected by Pancritius, in twenty-seven albuminuria was observed.

Pleurisy has been observed during the secondary stage, or quite late in the disease. It may occur along with the secondary eruptions with the usual symptoms. It may be dry or attended with moderate effusion. Sometimes there is a severe pain in the side, and there may be intense dyspnœa and fever. Pleurisy is often accompanied by joint affections.

Genito-urinary organs.—*Renal disease.*—Small gummata are occasionally observed in the kidneys, generally in association with gummata in the liver or elsewhere. Very rarely a gummatous infiltration may produce a large renal tumour. Nephritis occasionally occurs in the patients who are, or have been, the subjects of syphilis; but it is doubtful whether such cases are specific. Amyloid disease of the kidneys is sometimes a consequence of syphilis.

Testicle.—The testicle is not uncommonly affected in the early tertiary stage. There is a painless uniform enlargement of the body of the organ. There is often an accompanying hydrocele, which, as a rule, is not considerable. The surface of the organ remains quite smooth, although in a few cases small masses of induration may be felt at an early stage. The epididymis is very rarely affected, and the cord remains healthy. The enlargement is often considerable, and the organ may reach the size of a man's fist. Hutchinson remarks that when the tumour is large it feels very light in the hand, but this feature is by no means constant. The smoothness and hardness and the absence of pain are the most important points. Both organs may be affected.

The nervous system.—*Frequency.*—It has been estimated that the brain is affected in from 12 to 21 per cent. of patients who have tertiary symptoms, and in from $1\frac{1}{2}$ to $2\frac{1}{2}$ per cent. of all infected with primary disease.

Time of occurrence.—This may be as early as the sixth month, or as late as the twentieth year from infection. The first year has more cases than subsequent years, the number gradually diminishing with each year. It has been estimated that 40 per cent. of the cases of cerebro-spinal syphilis

occur within two years of infection. Of the lesions connected with occlu-
sion of vessels, 25 per cent. occur during the first two years. The earliest
case observed by Gowers happened three months after infection.

Sex.—Men are more frequently affected than women, as they are with
syphilis in general.

Dissipation, alcoholic and sexual excesses, anxiety, mental strain,
injury to the head, together with the inheritance of nervous instability,
predispose to a cerebral localisation of syphilis. Early efficient mercurial
treatment probably saves many from cerebral symptoms. It is well recog-
nised that the nervous system is relatively more frequently affected in
slight cases which have passed untreated.

Following Gowers, we may classify the lesions of the nervous system
produced by syphilis as—Inflammatory or congestive; resulting from a
process of tissue formation; and system diseases.

The inflammatory lesions are chiefly meningeal, with hyperplasia as
their characteristic feature. Much new tissue, with a gelatinous appear-
ance, is produced, which may either become fibrous or caseate. Either the
external or the internal membrane may be affected. Pachymeningitis
is more common in the inherited form than in the acquired. In the pia
mater the inflammation is usually local, and the new tissue is abundant.
In the spinal cord the pia mater is seldom affected alone. The meningitis
is frequently cerebro-spinal. Inflammation of the substance of the brain
occurs very early, but a case of chronic disseminated inflammation has
been described by Charcot and Gombault. The nerves, especially the
cranial nerves, may be the seat of syphilitic inflammation, in which case
there is cellular growth and infiltration of leucocytes in the sheath and
interstitial tissue. The optic nerves and the motor nerves of the eyes
are specially prone to neuritis. Cases of polyneuritis and neuritis of
individual nerves, such as the ulnar, have been recorded. The nerves may
also be affected in meningeal lesions, or they may be compressed by swell-
ing in bony foramina, by aneurysms of syphilitic origin, or by gummata.
Syphilis, moreover, predisposes to degeneration of the nuclei of the nerves.

A form of disseminated subacute myelitis, in which defined islets of
inflammation occupy the white substance of the cord, especially near the
surface, has been described by Julliard and Perret.

Under the heading of lesions resulting from a process of tissue
formation, must first be mentioned the occlusion of cerebral arteries by
syphilitic disease. The large vessels at the base are those most frequently
affected, and their occlusion leads to extensive softening of the cerebral
tissue.

Gummata grow commonly from the pia mater, and compress and
invade the substance of the brain or cord. They are rare within the sub-
stance of the brain or on the cranial nerves, although cases have been
recorded in which they were symmetrically situated on the latter. The
dura mater is generally adherent to the tumour, and a diffuse form of
gumma is sometimes met with growing from this membrane. Gummata
are generally superficial in the cerebral hemispheres or the pons. They
seldom invade the cerebellum or corpus striatum, but occasionally the
growth finds its way beneath the optic thalamus, spreading by extension
from the crus.

It is unnecessary to repeat the description which has been given of the
morbid anatomy of a gumma generally. The irregularity of shape and of
caseation helps to distinguish it from tubercle. While the gumma does

not infiltrate the neighbouring brain substance, it produces softening and displacement.

The symptoms are like those of any other tumour, and are general and local. The course of the malady is subacute or subchronic; and cerebral symptoms of very long duration are not likely to be produced by syphilis. Optic neuritis, when present, is always acute, and may be intense. A chronic form of optic neuritis is opposed to a diagnosis of syphilitic growth. The seat of the gumma being superficial, symptoms of cortical irritation are more frequent than in the case of other tumours. Convulsions are common. The oculomotor nerves are frequently involved, or there may be affection of smell or hearing.

The relations of tabes and general paralysis to syphilis must be left for discussion elsewhere; but there appears to be a large amount of evidence as to the causal relations of syphilis with these affections.

Occlusion of vessels produces a sudden focal lesion. Hemiplegia is the most common effect. This may be slight and transitory, or severe and permanent. The onset of complete occlusion is seldom attended by loss of consciousness. It is often preceded by headache, which may last for a few days, weeks, or months. The pain may be severe, and it may be general, or limited to the site of the lesion. When the basilar artery is occluded, there is very profound nervous disturbance, with coma, bulbar symtoms, bilateral paralysis, and rapid rise of temperature.

The headache of cerebral syphilis has certain peculiarities, which may be briefly enumerated. The pain is deeply seated, and constrictive or hammering. It may be localised or diffused, but is seldom general over the whole head. Its characteristics are its intensity, its nocturnal exacerbations, and its long duration and relapses. Nocturnal exacerbations may, however, be conspicuous by their absence. Insomnia is a frequent symptom, and when associated with headache should excite a suspicion of syphilis.

Epileptic attacks are common symptoms. They possess in themselves no special diagnostic features, and their syphilitic origin is generally borne out by the history and the association with other symptoms not usually present in ordinary epilepsy.

The symptoms produced by chronic syphilitic meningitis indicate a surface lesion. There are no signs of any considerable loss of function.

Hutchinson has called attention to cases in which myelitis appears to attack the lower part of the spinal cord during the secondary stage of syphilis. Gowers points out that syphilitic lesions of vessels so small as those of the spinal cord are unknown. The myelitis is probably produced by the toxine of syphilis. A temporary condition of paraplegia, affecting the sphincters as well as both sensation and motion in the lower extremities, may ensue. The upper extremities are usually unaffected. It is generally amenable to vigorous treatment, and does not relapse. Paraplegia may occur during the tertiary period, from various causes, such as gummata, etc.

There are two important elements in the diagnosis of cerebral syphilis, which have been emphasised by Gowers—first, the course of the symptoms; and, second, the probable seat of the lesion or lesions. As regards the course, true specific lesions are generally subacute or subchronic. Symptoms of certainly specific lesions rarely develop to a considerable degree in less than a week. On the other hand, they are very seldom actually chronic, and do not often take longer than three months to develop. An actually sudden onset is not at all uncommon, and is the

usual event in vascular occlusion. When symptoms come to a climax in a few days, or take many months to develop, it is not likely that they are due to a specific lesion. Important help may also be derived from a knowledge of the usual seat of syphilitic lesions. Syphilitic processes being outside the nerve elements, have no special relation to nerve function. Hence their effects are random in their distribution, and are only related to special function, when that function is subserved by one region.

The diagnosis of occlusion of vessels is assisted by the consideration that such symptoms as are present are seldom produced before the age of 45, except from embolism. Embolism is extremely unlikely in the absence of valvular disease of the heart. After the age of 45 the difficulties of diagnosis are greatly increased, for we have to consider the possibilities of occlusion from atheroma, etc.

The diagnosis of syphilitic paraplegia must be effected from the history and the presence of other signs of syphilis.

The results of treatment may confirm the diagnosis. There should be considerable diminution in the symptoms within from six to ten weeks, as far as these are directly due to specific processes. Treatment, however, can have no effect on such lesions as are due to blocking of vessels, or when nerve elements have been destroyed by the contraction of new fibrous tissue.

The prognosis is best in the case of gummata, and worst in the case of occlusion of vessels. According to the estimate of Mickle, about 50 per cent. of the cases recover more or less completely; probably from 25 to 35 per cent. die, and the remainder survive with grave nervous disorder. Hutchinson has recently stated that in his experience paraplegia, as occurring during the first two years of syphilis, is nearly always recovered from, and never relapses, and that, as regards patients affected with hemiplegia, they nearly all recover their health although permanently hemiplegic.

Life assurance in relation to syphilis.—The practice of life assurance offices varies considerably in regard to the acceptance of lives in which there is a history of syphilis. Jonathan Hutchinson, at a discussion at the Life Assurance Medical Officers' Association in 1896 on this subject, stated his opinion that, on the whole, the extra risk in cases of syphilis, in otherwise healthy persons, was a very slight one. In the case of a man with a primary sore who was in good health, and likely to submit to judicious treatment, he considered that there were no extraordinary risks to be run. In the secondary period, unless the case was quite exceptional, he would not consider the expectation of life to be below the average. The practice, however, with most offices, is to postpone any case in which there are signs of active syphilis, and to add an extra of from three to seven years in cases in which there is a history of primary syphilis during the five years preceding the proposal.

Prophylaxis.—The best prophylactic is chastity. The danger of contracting syphilis can be greatly diminished by personal cleanliness, and the systematic use of soap, warm water, and antiseptics, together with vaginal douches in the case of the female. That cleanliness alone is by no means a certain preventive, is shown by the frequent occurrence of syphilis in the higher grades of society. The spread of syphilis is undoubtedly promoted among the lower classes by neglect of personal cleanliness in both sexes. Every person who has syphilis in an active form should be warned as to the dangers of inoculating another person with the disease.

Marriage in relation to syphilis.—If an infected person has been for a

period of at least two years without symptoms of any kind, he may be permitted to marry. The risk that he will communicate syphilis to his wife, or to his offspring, after that period, is extremely small.

Treatment.—There are two drugs whose action on syphilis and its lesions is specific. These are mercury and iodide of potassium, the first being specially valuable in the earlier, the second in the later stages. We shall consider the treatment in the primary stage and in the secondary and tertiary stages separately.

The primary stage.—The excision of the chancre was recommended by Hüter, Auspitz, and Unna. We have seen that the vessels and lymphatics in connection with the chancre are involved at a very early period, and, accordingly, removal of the chancre cannot arrest the disease. I agree with R. W. Taylor in believing that no single case of syphilis was ever aborted or annihilated by early surgical procedure of any kind.

The presence of a chancre always indicates the necessity for local cleanliness. The parts should be frequently washed with warm water containing a drachm of boric acid to the pint, or mercurial washes may be employed, such as solution of corrosive sublimate (1 in 2000), or black or yellow wash, or solution of sulphate of zinc (2 grs. to the oz.). Should the sore become angry, iodoform powder may be locally applied.

There is a wide diversity of opinion as to the advisability of administering mercury at this stage. Many authorities consider, and with these we agree, that where there is an undoubted indurated chancre, mercurial treatment should be immediately commenced. Taylor holds that early treatment with mercury only delays the appearance of secondary manifestations for a longer or shorter time, and, as a rule, does not lessen the severity or extent of their distribution, and in many cases seems to render them more severe. He is convinced that it is by far the best plan to wait until the onset of the secondary stage before beginning a mercurial course. Jonathan Hutchinson, on the other hand, is of opinion that it is quite possible, by the early and continuous use of mercury, to suppress the secondary stage, or, in other words, to make it abortive. He states that in exceedingly few cases, where it has been possible to use mercury without interruption from an early period, has he known a well-characterised secondary eruption or a typical sore throat to occur. All are agreed that when the local condition is troublesome, attended by indurating œdema, etc., mercury should be started at once. There is no doubt, however, that, as a general rule, before mercurial treatment is started it is of the greatest importance to be certain of the diagnosis. The absence of secondary symptoms is not an unmixed good, if, as the result, the medical attendant or the patient is left in doubt as to the nature of the malady. As Taylor remarks, it is most salutary for the syphilitic to be convinced beyond any doubt that he is syphilitic. In the case of a sore the nature of which is doubtful, mercurial treatment should be reserved for the appearance of the secondary stage.

It is important at an early stage that the patient should be put into a proper condition for a course of mercury. A careful general examination of the patient should be made, so that the practitioner may have a thorough knowledge of his constitution and general state of health. The teeth should be inspected, and any that are carious appropriately treated. Smoking should be prohibited and moderation in alcohol enjoined. Sexual intercourse, it is needless to say, must be forbidden, as long as there is any risk to be run by the second party. The condition of the skin may be improved by a course of Turkish baths.

The secondary and tertiary periods.—All authorities admit the need for mercury during the secondary period, but opinions differ as to dosage, mode of administration, and duration of treatment. There are four methods in which mercury may be used—internal administration, inunction, fumigation, and hypodermic injection. The remedy may be given only when symptoms are present; or at intervals over several years; or continuously, for six months or several years.

The plan of giving mercurials only during the period when syphilitic symptoms show themselves, was recommended by Diday. Unfortunately one sees only too frequently how inefficient such treatment is. In spite of repeated warnings, hospital patients often only submit themselves to treatment while there are active symptoms. It is in these cases that one sees the worst forms of syphilis.

The interrupted mode of treatment was introduced by Fournier. The patient is treated with mercurials for two months, and then goes a month without. He is again treated with mercurials for two months, has three months' respite, and again has two months' treatment, followed by three months' respite, symptoms or no symptoms. In two years the patient has ten months with and fourteen months without treatment. In the third and fourth years the patient has four courses of treatment lasting six weeks, with intervals of equal duration. In the fifth year three courses are given. The preparation of mercury preferred by Fournier is the green iodide, which may be given in divided doses amounting to $\frac{3}{4}$ to $1\frac{1}{2}$ gr. daily.

The short continuous treatment was that pursued by Ricord, who recommended active treatment with mercury for six months, followed by iodide of potassium for three months longer.

The prolonged continuous treatment is that which has the support of Hutchinson in this country and Keyes in America, and is carried out by a large number of practitioners. Hutchinson uses small doses of grey powder; Keyes, the green iodide. Hutchinson recommends 1 gr. doses in pill, in combination with opium (gr. $\frac{1}{8}$ or $\frac{1}{4}$), repeated as frequently as the patient can bear it; the problem being to introduce as much mercury as possible without producing salivation or diarrhœa. Salivation must be guarded against by hygiene of the teeth and the use of an alum mouthwash, while diarrhœa must be prevented by appropriate diet and small doses of opium. The 1 gr. pill may be taken four, five, six, or even seven times a day, without reference to meals.

Keyes recommends that, to commence with, a granule ($\frac{1}{8}$ gr.) of the green iodide should be given three times a day. The dose should be gradually increased to four, five, six, etc., granules a day, until a dose is reached when the gums become slightly affected or diarrhœa sets in. This daily dose should not be exceeded, and may be continued with the aid of opiates and unirritating food, until active symptoms have disappeared, when the dose may be reduced to half, but should be at once increased if symptoms again appear.

Blue pill in doses of 1 to 3 grs., the tannate or gallate of mercury in doses of half a grain, and the biniodide in doses of $\frac{1}{16}$ to $\frac{1}{8}$ gr., are the most usual preparations of mercury given by the mouth, in addition to the grey powder and the green iodide already mentioned. ·Corrosive sublimate in the form of the liquor (dose, 1 drm.) is frequently given in combination with iodide of potassium in the later stages.

Iodide of potassium is as valuable in the period of periosteal nodes,

tertiary eruptions, and gummata, as mercury is in the earlier periods. It may be administered in doses of from 3 to 20 grs. three times a day, either with or without mercury. It is not, as a rule, indicated in the secondary stage, but even then should be given if cerebral complications arise.

Individual cases of syphilis must be treated according to their special features; and while ordinary mild cases may do exceedingly well on the continuous treatment with small doses given by the mouth, cases will every now and then be met with which call for other measures. Thus, when mercury by the mouth upsets the stomach or causes diarrhœa, then inunction, fumigation, etc., may be adopted with advantage.

The method of inunction is preferred to that of internal administration by many practitioners of great experience, as being more active, certain, and speedy in its effects. The blue ointment is the favourite application. It should be freshly made. The amount used at each application should be from 40 to 50 grs. It should be well rubbed in, the process taking about half an hour. The part rubbed should be changed daily, so that every part of the body in turn has its share of the application. The inunction should be preceded by a bath, and if a professional rubber can be obtained, it is better. If the patient is occupied during the day, the application should be made in the evening, otherwise the morning is the best time. Oleate of mercury has also been used for inunction, in strengths varying between 5 and 20 per cent., but has not, on the whole, proved so suitable as the blue ointment. Lately, mercurial soaps have been employed. A lather is made with these, which is applied, and allowed to dry on the skin.

Fumigation is another means of obtaining the rapid action of mercury, and may be used in obstinate and severe cases with advantage. Twenty to forty grs. of calomel or cinnabar are put in a small vessel suspended over the flame of a small lamp, and, together with a pan of boiling water, are placed under a chair, on which the patient sits covered with blankets. The duration of the bath should be from twenty to thirty minutes. It may be taken every other day, just before bed-time.

The principal forms of hypodermic intramuscular and intravenous injections are suspensions of calomel or yellow oxide of mercury, and solutions of corrosive sublimate. The method is one which cannot be recommended for routine use, and must be considered a measure to be used in cases of emergency, such as ocular, aural, and cerebral syphilis. Pure calomel is administered in 1 gr. doses, suspended in 10 minims of pure glycerin, glycerin and water, or mucilage of acacia, or in combination with 1 gr. of sodium chloride and 10 minims of water. Calomel injections are generally painful, and often give rise to abscesses and troublesome subcutaneous lesions. The yellow oxide of mercury is given in 2 gr. doses, suspended with half a gr. of acacia in 60 minims of water. It is said to be less painful and less frequently followed by local lesions than calomel. Perchloride of mercury is given hypodermically in doses of a tenth to an eighth of a grain dissolved in ten or twelve drops of water. All these injections should be made deeply into the subcutaneous tissue and not into the *cutis vera.* Necrosis of the skin is likely to follow if the injections are too superficial. The best situation for injections is the subcutaneous tissue of the buttocks, especially the depressions behind the great trochanters. The injections may be made every second day. The treatment is not well borne by women and children. The perchloride injections are, on the whole, the most satisfactory, and are valuable where a prompt action is desired. They

are rarely followed by abscesses. Pain at the seat of injection, infiltration, and local erythema are the most serious consequences. Great care should always be exercised that the injections are given with the strictest antiseptic precautions.

Intramuscular injections of the double chloride of mercury and ammonia (sal alembroth) have been highly spoken of by some surgeons in this country, especially Bloxam. A solution is used, containing 2 grs. of perchloride of mercury and 1 gr. of chloride of ammonium in 1 drm. of water. Ten minims of this solution are injected deeply into the gluteus maximus muscle once a week. Intravenous injections were introduced by Baccelli, who employed solutions of perchloride. This method has been largely used by continental surgeons, but not much in this country. Chopping speaks very favourably of the use of a 1 per cent. solution of the cyanide of mercury, of which 20 minims are introduced into the vein of the forearm in the direction of the blood stream. A rubber tourniquet is kept applied to the upper part of the arm until the needle has entered the vein, when it is removed and the injection then made. The injection is repeated daily. Those who have employed the method maintain that it brings about a more rapid and certain cure than any other plan of treatment.

Serum treatment.—Of late years treatment by means of injections of serum, obtained from an individual previously affected by the disease, has been tried, and some have obtained good results, both in the primary lesion and in secondary syphilis. The serum from an individual with well-marked secondary syphilis has been found to have more powerful antitoxic properties than one from an individual with tertiary symptoms. The serum of horses, mercurialised previous to bleeding, has also been tried, but has not been found to be beneficial, if it is not positively harmful.

Whatever mode of treatment is employed, an endeavour should be made to keep up the patient's general health. Good food, early hours, fresh air, and change of air and scene, are all-important aids in treatment. In chronic cases, an occasional course at Aix-la-Chapelle will prove of service. A sea-voyage, or bracing sea-air, will greatly benefit where there is much debility.

Hereditary syphilis, as a rule, requires prolonged and active treatment. A pregnant woman should be actively treated, not only when she is herself syphilitic, but also when the father of her child is syphilitic, although she herself may manifest no signs of the disease. Inunction and hypodermic injections of mercurial preparations, as already described, are more effective than other methods when the mother is syphilitic, but when the mother is healthy small continuous doses should be given. In any case the treatment should be commenced soon after the onset of pregnancy, and should be continued during its whole duration. The same treatment may be carried out during lactation. Both mercury and iodide of potassium have been found in the milk, when these drugs are administered to the mother. Grey powder is the most suitable form of administration of mercury to infants. It may be given in doses of one-eighth to one-third of a grain three times a day. The green iodide of mercury is also a useful preparation. To commence with, one-twentieth of a grain may be given, and the dose may be gradually increased to a quarter of a grain. Corrosive sublimate is also a favourite preparation with some authorities. Inunctions may be used with benefit in later stages. In the more severe cases of hereditary syphilis, even minute doses of mercury sometimes seem to hasten the fatal end. In

these, mercury must be given with the greatest caution, and the feeding of the child must be seen to with the greatest care.

<div align="right">HECTOR MACKENZIE.</div>

TUBERCULOSIS.

A SPECIFIC parasitic disease caused by a definite micro-organism, the *B. tuberculosis,* and characterised anatomically by the presence of minute bodies called tubercles, which tend to coalesce, to caseate, to soften, or to undergo fibrous or calcareous changes. The disease may be local, and limited to one organ or tissue, or it may be generally disseminated throughout the body.

The disease is always due to infection, directly or indirectly, from pre-existing cases, either in man or the lower animals. It is not always itself infectious. It only becomes certainly infectious when there is a communication between the diseased part and the exterior of the body, through which the infective material may be discharged.

History.—Tuberculosis is by far the most important disease to which the human race is subject. It attacks a third, or, as some have estimated, half the population of European countries, and kills a sixth part of the whole race. It prevails in almost every part of the world, among all races and all conditions of men. It exists to a wide extent among domesticated animals, and in some of these proves as fatal as it is in man. It invades every organ and every tissue of the body, but has a special affinity for the respiratory tract. Through the latter the micro-organisms most usually invade the body. In the lungs they multiply, set up fresh colonies, and from thence are discharged from the body by expectoration, and, thus set free, are again able to enter a fresh host.

In its pulmonary form the malady was known to the ancients, and was described by Hippocrates. The name of phthisis was given to it, on account of the wasting of the body which was observed to be the usual result of the disease. A graphic description of the physiognomy of the patient in an advanced stage of the disease was given by Aretæus, and could be little improved on in the present day. It was observed that the wasting of the body was accompanied by wasting of the lungs. It was not until the seventeenth and eighteenth centuries that any useful knowledge of the anatomical changes met with in phthisis was acquired, and that the small round bodies found in the lesions began to be described as tubercles. Matthew Baillie, in 1793, gave a clear description of tubercles— " Rounded firm white bodies, at first very small, not larger than the heads of very small pins, and in this case frequently accumulated in small clusters. The small tubercles of a cluster grow together and form one larger cluster." The caseation of these bodies, the softening of their centres, and finally the formation of abscesses and cavities in the lungs, were accurately observed. The relation of caseous tubercle in the lung to caseous tumours in the neck and elsewhere, which were designated scrofula, began to be discussed.

The great advances in a knowledge of the disease date from the nineteenth century. Three men deserving of special honour stand out from all others who have laboured in this field. These are Laënnec, Villemin, and Koch. Laënnec (1819) taught the unity of tubercle in its various forms and situations, and, by the discovery of auscultation, made it possible

to detect the presence of the lesions set up in the lungs by tubercle, as had never been the case before. Villemin (1865) proved the inoculability of tubercle on the lower animals; and finally Robert Koch (1882) announced the discovery of the *B. tuberculosis,* and by masterly methods proved the bacillus to be the cause of the disease, and demonstrated the unity of all the various forms of tuberculosis. Thus the local form of tubercle, which was for a long time thought to be a distinct malady, and was described under the name of scrofula, and phthisis which was regarded as typically a constitutional disease, the result of a diathesis, were both seen to be simply different forms of the same disease.

Predisposing causes.—Constitution.—It has been a belief handed down from the time of Hippocrates, that certain constitutional peculiarities render individuals more susceptible to phthisis. A clear, delicate skin, pink and white complexion, fine silky hair, long eyelashes, bright eyes, tapering fingers, and precocity of intellect, are some of the general characteristics which have been thought to point to vulnerability to tuberculosis. Landouzy has recently revived the idea that individuals with red hair, with blue eyes and fair skin, are specially liable to tubercle. Such persons he euphemistically calls "Venetians." Certain peculiarities in the shape of the chest have been also associated with phthisis. In a typical form the upper ribs are straight, and their interspaces widened, the lower ribs oblique, and their interspaces narrowed, the whole chest being long and narrow, and flat from before backwards. The clavicles, too, are prominent at their acromial ends, while the scapulæ project like wings. In other cases, the chest is long, narrow, and rounded, and the diaphragm relatively high. These types of chest are perhaps more often the results of the disease than its predisposing causes. Lanky overgrown young adults often fall a prey to tubercle, but perfect physique appears to form no barrier to its development.

Sex.—The influence of sex has been variously estimated by different observers. Laennec and other authorities since his time have stated that women are more subject than men to pulmonary tuberculosis. The general experience in London is that the reverse is the case, and more men than women suffer from the disease. Thus, out of 1562 out-patients under my care at the Brompton Hospital, affected with pulmonary tuberculosis, 904 were males and 658 females, giving a proportion of 100 males to 73 females. This proportion tallies closely with that of male and female deaths from pulmonary tuberculosis, as given in the Registrar-General's reports. The mean annual death-rate in a standard million from phthisis, 1881–90, was in London, for males, 2247, and for females, 1580. For the whole of England and Wales during the same period the rate was 1847 males to 1609 females. This shows that for the whole country more males than females are affected by pulmonary tuberculosis.

The remarks of Tatham on this point are of great interest and importance. He says: "From the year 1851 to 1865 the phthisis rate was greater among females than among males, although the difference gradually diminished as time went on. Ever since the year 1866, however, the mortality has been uniformly in excess, not among females as formerly, but among males; and in the last two decennia the excess of the male-rate over the female-rate was greater than had been the excess of the female-rate in the decennium 1851–60. From information obtained since 1890, it has been ascertained that a similar change in the sex-incidence of phthisis mortality is still going on." Thus, while the female-rate to the male-rate,

taken as 1000, in 1851–60 was 1076, in 1861–70 it was 1006, in 1871–80, 918, and in 1881–90, 871. " In the decennium, 1881–90, in twenty-four counties, containing more than three-fourths of the entire population of England and Wales, the male death-rates were in excess of the female, while in the remaining twenty-one counties, containing less than one-fourth of the population, the female-rates were in excess of the male-rates." " As in the case of phthisis," Tatham adds, " the mortality from other tuberculous diseases is considerably higher among males than among females."

Age.—Tuberculosis manifests itself at all ages. In the young it tends to affect the glands, or to distribute itself widely throughout the body; in the adolescent or adult it more commonly locates itself in the lungs in the form of chronic pulmonary phthisis. The greatest prevalence of phthisis is in the adult, between the ages of 20 and 45, while other forms of tuberculosis flourish most widely in children under 5.

Annual Mortality per Million living at all Ages, and at Eleven Groups of Ages in Three Decennia.

			All Ages.	0–	5–	10–	15–	20–	25–	35–	45–	55–	65–	75 and Upwards
			Phthisis.											
1861–70	Persons		2475	968	454	825	2651	3928	4243	4026	3340	2656	1603	539
1871–80			2116	767	358	664	2086	3117	3619	3745	3132	2449	1476	492
1881–90			1724	536	290	521	1545	2324	2901	3132	2737	2169	1355	521
			Other Tuberculous Diseases.											
1861–70	Persons		765	4477	525	269	182	125	90	76	88	111	121	78
1871–80			747	4442	503	256	169	104	74	62	65	80	96	45
1881–90			696	3963	554	306	229	171	123	107	94	94	83	48

For males, the largest rate of mortality from phthisis exists between the ages 35 and 45, and for females between 25 and 35. In the case of other tuberculous diseases, by far the heaviest mortality is found under the age of 5, from which period it gradually diminishes. It is popularly supposed that the liability to pulmonary tuberculosis diminishes with age, and that it is seldom contracted after 50. The tables which we give from the Registrar-General's Reports show the prevalence of the disease in late as well as early life.

Heredity.—Tuberculosis is pre-eminently considered to be a hereditary disease. It has been shown over and over again that a larger proportion of cases of tuberculosis occurs among the children of phthisical parents than among the offspring of the non-phthisical.

The experience of all life assurance companies has been that among those with a family history of phthisis there is a heavier mortality than the normal. To protect themselves from loss, it is usual to charge extra premiums in such cases. The record of eighty families with hereditary

history was investigated with great care by Reginald Thompson. Out of 385 children, more than half were affected with tuberculosis. Out of 11,041 cases of phthisis, collected by various investigators, there were 3084 in which one or both parents were phthisical, giving a proportion of nearly 28 per cent. Out of 1205 cases under my own care, one or both parents were phthisical in 342, giving a proportion of 28·4. Of course, if one includes brothers, sisters, uncles, aunts, etc., the proportion of so-called hereditary cases will be still further increased, and it may be safely asserted that, in over a quarter of the cases of tuberculosis, there will be found a history of tubercle in the parents, and in a half of the cases in some member of the family.

It has been found that a larger proportion of women than of men in London have a family history of phthisis. Thus, out of 515 women under my care, one or both parents were phthisical in 180, or 35 per cent.; while in 690 males, one or both parents were phthisical in 162, or in 23·5 per cent. Squire similarly found, in 396 phthisical females, 37·9 per cent. with a history of phthisis in parents, and in 604 males, 29 per cent. Reginald Thompson, including collaterals as well as ancestors, found a family history in 58 per cent. of females, and in 36 per cent. of males. It will be found that, when one takes into account the greater prevalence of phthisis among males in London, that a family history is found in reality in quite as many males as females.

When we come to consider what is the meaning of heredity in phthisis, we here come on difficult and debatable ground. Before the knowledge of the dependence of the disease on a micro-organism, it was considered that the disease itself or a diathesis was actually inherited. It is now generally thought that what is inherited is not the disease itself, but a predisposition to it. In the case of the child of a phthisical parent, it is obvious that the chance of infection is very considerable. In the case where phthisis has occurred in a brother or a sister, the chance of exposure to a common cause of infection must be borne in mind. Baumgarten is almost alone in maintaining not only that the disease itself may be congenital, but that it generally is so. A large number of experiments have been made to determine whether tuberculosis might exist in a latent form in the newly born, in cases where there was no naked-eye evidence of tubercle. Fragments of the organs of the offspring of tuberculous mothers have been inoculated into guinea-pigs. In only three cases have the experiments proved successful. A few undoubted cases have recently been observed where women in an advanced stage of tuberculosis have given birth to tuberculous fœtuses, or infants which died soon after birth. In these cases both tubercles and bacilli have been found in the fœtal tissues, while bacilli have been discovered at the same time in the placenta and in the blood of the umbilical vein. Bang of Copenhagen, in a very few cases out of a large number examined, has found tubercle in the internal organs of the fœtuses of cows. M'Fadyean, of the Royal Veterinary College, London, stated in 1899 that he had seen only four undoubted cases of congenital tuberculosis in the calf, although he offered a premium for every case sent to him. It may therefore be accepted that fœtal tuberculosis, though possible, is an extremely rare event, and that the disease, in all but very exceptional cases, is acquired after birth. Everyone will admit that the children of tuberculous parents, especially among the poor, run a greater risk than others of acquiring the disease. What looks like heredity is often simply infection. It would

appear from C. T. Williams' experience of phthisis among the higher classes, that, as one would expect, heredity in them plays a smaller part. He found direct inheritance in 120 out of 1000 cases, or in only 12 per cent. Consanguinity, where both parents are of healthy stock, can have no effect, but where on both sides predisposition exists this will be increased in the offspring.

Trauma has been recognised as a predisposing cause of tuberculosis. An injury to a joint or to a lung may be followed by tubercle. It would seem that, as the result of the injury, the part was able to offer less resistance to the tubercle bacillus. Perroud has described a form of phthisis affecting boatmen on the Rhône, who, from constant strain, sustain a kind of chronic trauma of the lung. Mendelssohn has reported cases of phthisis as a sequel to contusion of the chest. Operations on tuberculous joints seem sometimes to set up a general tuberculosis, probably due to the bacilli gaining entrance to the circulation through wounded vessels.

Occupation.—The lower classes suffer more than the upper, which is explained by the different conditions under which they live, apart altogether from occupation. Those who lead outdoor lives are less liable than those who work indoors. Those who work in stuffy, crowded rooms, and those who work amid dust, such as grinders, masons, stone-cutters, workers in hair, etc., are the most liable.

Environment.—Crowded, dirty, and badly-ventilated dwellings must be considered as particularly potent in propagating the disease.

Alcoholism must be regarded as a powerful predisposing cause of tuberculosis. It is almost invariable to find tubercle present in the lungs in patients dying in the course of alcoholic paralysis. Tubercle of the peritoneum or pleura frequently complicates cirrhosis of the liver. I have found a history of alcoholic excess in a considerable proportion of my male phthisical cases. Dickinson, in comparing a number of alcoholic cases with a like number in which there was no history of drink, found a decidedly larger proportion of the former tuberculous. It would, indeed, be strange if it were otherwise. Alcohol in excess undermines the strongest constitution, and renders the body less resistant to disease of all kinds. This is specially true when the individual leads a sedentary town life. Considerable amounts of alcohol may be taken, without obvious deterioration of health, by persons who lead an out-of-door life and eat heartily.

Pregnancy has been held by some to retard the progress of pulmonary tuberculosis, by others to increase its risks and hasten the fatal termination. The evidence of different authorities has been fully detailed by Wilson Fox, who concludes that phthisis frequently originates during pregnancy, and that, when previously existing, it is aggravated by this state. Its course is often accelerated after parturition, although in some cases the symptoms are materially alleviated.

Previous disease.—Diabetes mellitus is frequently complicated with pulmonary tuberculosis. Such cases are, however, very rarely seen at the Brompton Hospital. Cancer is not very commonly met with among the tuberculous, probably for the reason that the age-incidence is at a different period of life, and not that there is any actual antagonism between them. In persons dying from cancer, a tuberculous lesion in the lungs is frequently met with. Syphilis, by undermining the constitution, increases the susceptibility to tuberculosis. Tuberculosis in a syphilitic subject usually runs an

unfavourable course. Pleurisy is generally considered as a predisposing cause, but we shall see that what is regarded as simple pleurisy is very frequently tuberculous, and therefore the occurrence of pleurisy is often only a manifestation that tubercle has already invaded the body. Chronic bronchitis not uncommonly appears to terminate in phthisis, but the question then sometimes arises whether tubercle has not been present all along. Pneumonia is but rarely followed by phthisis. Congenital heart disease is very often complicated with pulmonary tuberculosis. This is especially likely in pulmonary stenosis, in which tubercle of the lungs is a frequent termination. The lower vitality produced by the specific fevers must be regarded as a predisposing cause. Measles in children is especially apt to be followed by tubercle.

Other predisposing causes are prolonged lactation, insufficiency of food, and depressing moral emotions, which appear to render the body less resistant to bacilli.

Antagonism.—Certain diseases or morbid conditions are believed to exert an action antagonistic to tuberculosis. Of these, malaria is one of the most important. It is very doubtful whether such antagonism really exists. In malarious districts, tuberculosis is constantly mistaken for malaria. The comparative immunity from tuberculosis which has been recorded in such has probably depended on other causes. Mitral stenosis is only exceptionally associated with tubercle, but it is not clear that other forms of valvular disease are unfavourable to tubercle. Asthma and emphysema are also believed to be antagonistic to it. This is probably true as regards asthma, but emphysema frequently coexists with pulmonary tuberculosis. Chlorosis, plumbism, gout, and rheumatism are other conditions which are supposed to increase the resistance. Chlorosis and plumbism probably have no influence one way or the other. Gout and phthisis are seldom associated, but probably for the reason that the age incidence is different. Rheumatism certainly does not diminish the susceptibility to phthisis. A history of preceding rheumatism has been observed in from 10 to 18 per cent. of cases of phthisis.

Bacteriology.—**Character of bacilli.**—The bacilli of tubercle are short slender rods with rounded ends, measuring a quarter to half the diameter of a red blood corpuscle, 1·5 μ to 3·5 μ. Their apparent breadth is constant for the same method of staining, varying between 0·3 μ and 0·5 μ. As a rule they are slightly curved. They are usually solitary, but occasionally occur in pairs, or in short chains of three or four elements. The length of the bacillus varies with the culture. Thus the rods are shorter in young cultures than in old. Frequently the bacilli do not stain uniformly, but present a beaded appearance, due to the occurrence at regular intervals of ovoid, strongly refracting clear spaces, unaffected by the colouring agents. These clear spaces were considered by Koch, who first observed them, to be occupied by spores, the spores resisting the stain which coloured the general protoplasm of the bacillus. The prevailing opinion at the present time is that they are not spores but simply vacuoles, due to retrogressive changes. Some observers have found spheroidal bodies to be present, which stain more deeply and are more resistant to decolorisation than the rest of the bacillus. It has not as yet been successfully demonstrated that these bodies possess the biological characteristics of spores.

A description of the form of the bacillus would be incomplete without some reference to the variations which have been observed by Metchnikoff, Fischel, Coppen Jones, and others, in old cultures and in cultures grown

in special media. Metchnikoff has drawn attention to certain dwarf forms, occurring in cultures grown on serum or on glycerin jelly. These are extremely short bacilli, closely resembling micrococci. He has also found in avian cultures produced at a temperature of 43°·6 C. giant and ramifying forms. These are many times longer than the ordinary bacilli, and are clubbed at their extremities. In the older cultures branches are thrown out from the body of the bacillus, which similarly are club-shaped. Such forms have almost exclusively been found in cultures of avian tubercle, but Fischel and Bruns have observed the ramified forms also in the case of the mammalian bacillus. Fischel has also noted filament-like forms, with short lateral branches and sometimes forked extremities. Lubinski has described the formation in certain media of long threads. The existence of these exceptional forms suggests a possible relationship between the tubercle bacillus and cladothrix, or, as Coppen Jones thinks, between it and the ray fungus.

Staining of bacilli.—One of the most essential characteristics of the bacillus is the mode in which it reacts to staining reagents. It is stained by aniline dyes, such as fuchsine or methyl-violet, aided by a mordant, such as aniline oil or carbolic acid, and resists decolorising by dilute acids. This property of resistance to decolorising serves to distinguish it from all other bacilli known to produce disease, except that of leprosy. The leprosy bacillus is stained much more readily and rapidly than the tubercle bacillus, which latter stains slowly, or requires the aid of heat to hasten the process. The mode in which the leprosy bacillus is grouped in clusters in the interior of special cells also distinguishes it from the tubercle bacillus. It resists better than the tubercle bacillus the decolorising action of hypochlorite of sodium. The smegma bacillus closely resembles the tubercle bacillus, but is much more readily decolorised after staining. Further particulars regarding it are given in the section on renal and vesical tuberculosis. Recently L. Rabinowitsch has discovered a bacillus which is very frequently present in butter, and is similar both morphologically and in its staining reactions to the tubercle bacillus. It differs from it, however, in its cultural properties, and in the lesions produced on inoculation, which more resemble those of glanders than those of tuberculosis. Although pathogenic for guinea-pigs, it is not pathogenic for rabbits or mice, and infected animals do not react to tuberculin. The bacillus recently found by Möller on timothy and other grasses, and in the fæces of cows, horses, swine, goats, and mules, also closely resembles both the tubercle bacillus and the butter bacillus. It has not been shown that these bacilli are pathogenic to man.

The interval which elapsed between the discovery of the bacillus of anthrax and that of tuberculosis showed that there must be some special difficulties in staining the latter. The aniline dyes methylene-blue and methyl-violet had been found to stain all micro-organisms, so far known, without difficulty; but until applied in a special way by Koch, they did not stain the *B. tuberculosis*. Koch had observed that the addition of alkali to methylene-blue facilitated the coloration of various micro-organisms, and in this way succeeded in staining the tubercle bacillus, and rendering it visible for the first time. The process of staining was greatly improved and simplified by Ehrlich, who showed that the combination of an aqueous solution of aniline oil with an aniline dye, such as methyl-violet, formed a fluid which stained the bacillus, and that the bacillus so stained resisted decolorising by means of dilute acid.

Various attempts have been made to explain the cause of the difficulty

of staining the bacillus. It was supposed that it depended on the presence of an envelope which was naturally very resistant to the stain, and that this envelope was altered by an alkali or aniline oil so as to admit the stain to the interior. The envelope similarly prevented the penetration of the decolorising acid to the interior. The existence of an envelope endowed with special characteristics is a pure hypothesis. Later investigations have shown that the *B. tuberculosis* differs from others as regards staining only in the greater difficulty with which it takes the stain, and the corresponding difficulty with which the stain can be removed.

A great many modifications have been made in the method of staining, which has thereby been much simplified. Aniline reds, such as fuchsin or rubin, have been found more practically useful than methyl-violet. One of the most convenient methods of staining is that of Ziehl, as modified by Neelsen. The staining fluid employed is composed as follows :—

Fuchsin	1gr.
Phenol	5gr.
Distilled water	100gr.
Absolute alcohol	10gr.

In examining sputum for bacilli, a small yellow mass should be picked out by means of a platinum needle. This should be placed between two cover-glasses, and evenly distributed over their surfaces by slight pressure. The cover-glasses are then separated. The films are allowed to dry, and the glasses are then passed two or three times through the flame of a spirit-lamp to fix the films. The staining fluid may then be poured on the cover-glass, or the latter may be placed face down on the surface of the fluid. In either case, heat should be gently applied until the fluid steams. Staining is effected in four minutes when the fluid is heated, but takes considerably longer at ordinary temperatures. The cover-glass is then washed with water. Next, to decolorise it, it is placed for a minute or two in a 25 per cent. solution of sulphuric acid or nitric acid. It is then washed in dilute alcohol to remove the fuchsine set free by the acid. The bacilli are then alone left coloured. A weak solution of methylene-blue may be used as a counter-stain, and when washed again in water, the preparation is ready for examination. The staining of bacilli in the tissues is a more difficult matter. In this case it is better to avoid heating, to use the staining fluid cold, and to allow it to act for twelve to twenty-four hours.

Natural history of the bacilli.—The biology of the bacillus is of even greater importance than its morphology. The principal biological characters of the *B. tuberculosis* are that it is parasitic, aërobic, and non-motile, growing most readily at a temperature of about 37° C. It is a facultative anaerobic, and probably also a facultative saprophyte. From an etiological point of view it is of the highest consequence to know under what conditions, on the one hand, the bacillus will grow, multiply, and flourish; and, on the other, what influences will check or destroy its vegetability or alter its virulence. The organism which it was found difficult to stain was also found difficult to cultivate. In order to establish the rôle which the bacillus plays in the causation of the disease, it was necessary to obtain pure cultivations in some medium outside the body, and to show that such pure cultivations were able, equally with tuberculous products, to produce tuberculosis. After several failures, Koch succeeded in growing the bacillus in sterilised blood serum.

It was found to develop best at a temperature of 37° to 38° C. At a temperature over 42° it ceased to grow. At 30° the growth was

extremely attenuated, and was completely arrested between 28° and 29°. A point of extreme practical importance is that the bacillus is usually incapable of growing outside the body, except in artificial media kept at suitable temperatures. Solidified blood serum, glycerin agar (nutrient agar with 6 to 8 per cent. glycerin), and glycerin meat bouillon (such as veal broth with 5 per cent. of glycerin), are found to be the best media. It has also been successfully cultivated on potato and other vegetable media. It should be added that the most recent investigations go to show that the bacillus can live outside the animal body on dead organic matter. There is evidence that it may multiply in sputum outside the body. Delépine states that colonies of the mammalian bacillus will grow slowly in glycerinated media at the ordinary room temperature, both summer and winter, without losing their virulence. Ransome affirms that it is possible to grow the bacillus on wall-paper saturated with organic vapour from the breath at the ordinary room temperature.

The growth of the bacilli in blood serum is very slow. Except when the medium has been contaminated, no change occurs until one or two weeks after sowing. At the end of this interval little roundish granules of a dull white colour appear on the surface. These increase in volume, and at the end of another week become slightly prominent, and form dry, dull, greyish white scales. In the first cultures the scales generally remain isolated. Second and third cultures are prepared in the same way. It is not until the fourth or fifth generation that the cultures grow more rapidly, regularly, and abundantly, having become, so to speak, acclimatised to the media. Subsequent cultures are not composed simply of isolated scales but of confluent colonies. All the surface is covered with a thin, dry layer, studded with little prominences. The bacilli in multiplying do not develop in depth, but always at the surface. They never liquefy the serum, and always remain superficial. The liquid at the bottom of the tube is never rendered cloudy, even when fragments of the growth are detached and inserted in that position.

At the end of a month the cultures have generally acquired their maximum of development. The appearances of cultures, when examined under a low power of the microscope, are both interesting and characteristic. About the end of the first week after sowing, before any change is perceptible with the naked eye, sinuous lines may be observed on the surface. The smaller are like the letter S, the larger have been compared by Koch to the arabesques of ornamental writing. These curved figures are seen to be composed of bacilli arranged in columns. The bacilli, although close together, are separated from one another by clear spaces. Cultures appear to retain during many generations, without modification, the original properties of the bacillus. Cultures continued by Koch during nine years, external to the body of any animal, had preserved unchanged their properties, except for a slight diminution in virulence.

We have alluded to certain appearances in the bacilli which suggested the existence of spores. One of the main arguments against such being due to spores is that the bacilli in which they occur are not more resistant than other bacilli to the influence of heat, desiccation, etc. The fact that caseous matter in which bacilli cannot be recognised, is sometimes extremely virulent, suggests that spores are very probably present in it. It is possible that bacilli may be actually present in such material, and have been overlooked on account of their fewness. This, however, would not explain virulence. In old cultures but few bacilli may be found,

together with round granules which strongly fix the colouring matter. Sown on a suitable medium, such old cultures give rise to typical young cultures. It seems likely that the growth has resulted from the granules just mentioned. Similar granules are to be found in the virulent caseous material in which bacilli are absent, or at any rate cannot be detected.

Identity in different situations. — The identity of the bacillus in human and mammalian tubercle may now be considered to be established without a doubt. Besides producing exactly similar lesions when inoculated, they have the same form, appearance, and modes of staining and cultivation. It is otherwise, however, with the bacillus of avian tubercle, regarding the relation of which with the mammalian tubercle bacillus, a fierce controversy has been going on. The two bacilli are indistinguishable in form and colouring reaction. But although morphologically so much alike, there are such striking biological differences between the two, and such different effects from inoculation experiments, that there seems to be little doubt that they are entirely distinct. Koch says: "I do not hesitate to maintain that the bacilli of fowl tuberculosis are a species by themselves, but closely related to the (mammalian) tubercle bacilli."

While the mammalian bacillus cannot be cultivated at a temperature over 42° C., the avian flourishes at 43° C., and can be successfully cultivated at 45° C., and even above. There is a striking difference in the appearance and consistence of young cultures in solid media: the mammalian are greyish, coherent, dry, hard, and difficult to spread out evenly on a cover-glass; the avian are whitish, soft, moist, and easily spread out. Avian cultures preserve their vitality much longer than mammalian cultures. But the most striking differences exist in regard to their inoculability, which will be referred to later on.

Influence of surroundings on bacilli.—There is good reason to believe that the principal mode in which tuberculosis is spread is by the dissemination of dried sputum from the subjects of pulmonary tuberculosis. It is therefore necessary to know what is the effect of various circumstances and agencies on the vegetability and virulence of tubercle bacilli. A culture, 5 to 6 months old, can only exceptionally be recultivated; at the end of 8 to 12 months, recultivation is impossible. The virulence diminishes with the age of the culture, and cultures 8 to 12 months old produce the same effects as dead bacilli when inoculated.

Dried sputum containing tubercle bacilli has been shown to remain virulent for several months, but after a time the virulence gradually diminishes until it is finally lost. Bacilli retain their vitality for from two to four months when kept in sterilised water. Putrefaction, whether in air, in light or darkness, in water or underground, has no effect for a long time on the virulence of the bacillus. The carcases of tuberculous animals in an advanced condition of putrefaction have been found still to contain matter capable of producing tuberculosis by inoculation.

The bacilli offer great resistance to the action of gastric juice. They have been found still virulent after six hours' digestion, at a temperature of 38° C., in gastric juice, obtained through a fistula from the stomach of a healthy dog. Bacilli show great resistance to cold. Successive freezing and thawing for several weeks have been found to have no effect on the virulence of tuberculous material. A great many experiments have been carried out to determine the effect of heat on the vegetability and virulence of the bacillus. Dried bacilli are more resistant than moist to exposure to heat, and dry heat is less destructive than moist heat. It may be taken

as an established fact that an exposure for five minutes to the action of boiling water is sufficient to kill bacilli. Yersin found that exposure to moist heat at 70° C., or over, for ten minutes had this effect. Forster found that, while moist heat at 70° killed in five to ten minutes, at 60° forty-five to sixty minutes were required, and at 50° twelve hours had no effect.

Under the influence of heat, the vegetability disappears before the virulence. Woodhead states: "The most deadly tuberculous material can be rendered absolutely innocuous, so far as any spreading infective disease is concerned, by the action of a temperature at which water boils. We have evidence that a lower temperature than this is sufficient to bring about the same results when allowed to act for a longer time; but for the present it is sufficient to state that boiling for an instant even renders the tubercle bacillus absolutely innocuous." Woodhead found that artificial tuberculous milk, heated at 80° C. for ten minutes, was not always innocuous. One pig fed with such material became tuberculous. There are considerable discrepancies among the results obtained by different observers, and it is obvious that the effect of "boiling for an instant" may vary considerably, according as the processes of heating and subsequent cooling are slow or quick. There is no doubt, however, that for practical purposes Woodhead's contention is absolutely true.

Pasteurisation or sterilisation of milk cannot altogether be depended on to kill bacilli which may be contained in it. The temperature to which the milk is brought never reaches 95° C. Sunlight has a powerfully destructive action on bacilli. Exposure to the direct solar rays kills them in a few minutes or a few hours, according to the thickness of the stratum. Straus found that very abundant cultures were killed in two hours after exposure to the summer sun. Diffused daylight has also a powerful though slower effect. Exposure to it kills the bacilli in from five to seven days.

The influence of antiseptic agents on the bacillus has received much study. Koch has experimented with a number of these by adding them in small amounts to culture media. He found that the following, among others, hindered the growth of the bacillus when present even in very small doses, namely, a number of ethereal oils—β-naphthylamin, paratoluidin, xylidin; certain aniline dyes—fuchsine, gentian-violet, methylene-blue, etc; and among metals the vapour of mercury and salts of silver and gold. Compounds of cyanogen and gold were specially active; in a proportion of one part to one or two million parts of the culture medium they arrested the growth of the bacillus. All these substances remained without effect when tried on tuberculous animals. Yersin found carbolic acid, when applied directly to the bacilli, most deadly to them. Thus, 1 in 20 solution killed them in thirty seconds, and 1 in 100 in one minute. On the other hand, saturated solutions of creosote and naphthol had no effect in one hour. Schill and Fischer found that exposure of tuberculous sputum to the influence of various antiseptics for twenty hours had no effect in destroying its virulence. An exposure to a 3 per cent. solution of carbolic acid for twenty hours, or to absolute alcohol for ten hours, was found to be effective. The influence of sulphurous acid gas has been investigated by Vallin, who showed that bacilli exposed for fourteen hours to the gas produced by the combustion of 30 grms. of sulphur per cubic metre, were killed, while exposure for twenty-four hours to the gas produced by combustion of 20 grms. per cubic metre, failed to kill. Iodoform has been found by Stchégoleff to exercise *in vitro* an antagonistic action on the bacillus, but

experimental injections in animals of iodoform along with bacilli have had no deterrent effect.

Chemical constitution of bacilli.—By treating with a mixture of ether and alcohol, Hammerschlag found that bacilli, previously well washed and dried, lose 27 per cent. of their weight—a loss much greater than is experienced by any other microbe similarly dealt with. The extract so obtained is formed of fat and lecithin, and a toxic substance which, on injection, throws guinea-pigs and rabbits into convulsions and kills them. By treating the residue, insoluble in ether and alcohol, with a 1 per cent. solution of potash, there can be extracted an albuminoid substance. The substance which remains is probably cellulose. According to Koch, the bacilli contain two non-saturated fatty acids, one of which is soluble in dilute alcohol, and is easily saponified by the addition of soda, while the other only dissolves in boiling absolute alcohol or ether, and saponifies with great difficulty. These two acids are stained in the same way as the bacillus, form a continuous layer in its interior, and are the cause of its resistance to absorption in the animal body.

From pure cultures in a medium containing glycerin, Koch obtained a highly toxic extract which he called tuberculin. This substance was originally introduced as a remedy for tuberculosis, and in that aspect will be considered under the head of treatment. Koch was led to the discovery of tuberculin by observing the effects of the subcutaneous injection of dead bacilli on guinea-pigs, both healthy and tuberculous. He concluded that the tissues dissolved out something from the bacilli which had a powerful toxic action, and this principle he endeavoured to extract artificially.

The dead bacillus is not simply an inoffensive foreign body; it is a toxic body. Prudden and Hodenpyl have shown that dead bacilli, separated from such of their metabolic products as are set free in the culture media, or are extracted by prolonged boiling in water, or 50 per cent. glycerin, are capable of inducing marked effects on the body cells of the rabbit. Such dead bacilli are distinctly pyogenic, causing, when injected subcutaneously, localised suppuration. They are capable of stimulating the tissues about the suppurative foci, to the development of a new tissue closely resembling the diffuse tubercle tissue induced by the living microbe. There is, in the nodular structures thus produced, no tendency to caseation, and no evidence of proliferation of the bacilli, but rather a diminution of their number. These observers think it possible that a certain number of the miliary tubercles found in the body, after a generalisation of the tuberculous process from an old tuberculous focus, may actually be innocuous growths, or at least harmful only as foreign bodies in the tissues where they develop, and that the dense masses of fibrous tissue present in the lungs in cases of healed tuberculosis may be actually innocuous, and no longer capable of lighting up a fresh infection, although harbouring stainable bacilli. Tubercles may be the result of a conservative process, rendered futile by a destructive tendency to caseous degeneration, developed under the influence of a metabolic product of the living and growing germs which the tuberculous foci still harbour.

Straus and Gamaleia have worked at the same subject. Their conclusions are of great importance. They found that dead bacilli introduced into the body of an animal retained their aspect and colour reaction for months. The rule for other dead pathogenic micro-organisms, similarly introduced into the body of an animal, is that they rapidly disappear, and leave no trace behind. Dead bacilli introduced into the peritoneum, or

directly into the circulation, moreover produce lesions closely resembling those due to living bacilli. Even caseation, according to these observers, is not unusual. In the absence of anatomical lesions, dead bacilli are able to produce profound effects on the system, and bring about progressive emaciation, cachexia, and death.

The distribution of bacilli. — *Bacilli in the body.* — In the case of miliary tubercle, bacilli are in greatest abundance when the granulations are comparatively small and recent, and gradually diminish in number as caseation advances, when they are to be seen only at the periphery. The existence of bacilli in the blood has been demonstrated in a few cases of acute miliary tuberculosis.

In the case of chronic tuberculosis, the bacilli are relatively few in grey slowly growing tubercle, but they are particularly abundant in recent caseating and softening centres, and in the interior of cavities whose walls are rapidly breaking down. They are less numerous in older cavities with thick walls, and still fewer in parts affected with cicatricial induration.

Bacilli in the secretions and excretions. — Caseating and softening cavities in the lungs, it has just been pointed out, contain abundant tubercle bacilli, which, accordingly, are readily found in the sputum which is expectorated in cases where such cavities exist. The number of bacilli present in the sputum will vary according to the condition of the lungs, but in an active and progressive case it may be beyond calculation. In renal or vesical tuberculosis, bacilli may be found in the urine; in uterine tuberculosis, in the vaginal discharges; and in tuberculous ulceration of the intestines, in the fæcal evacuations. Neither the sweat nor the breath contains bacilli. In the case of the sweat, experimental inoculations have proved quite innocuous. Ransome has stated that he found bacilli in the condensed breath of a phthisical patient; and Giboux, that he gave tuberculosis to two rabbits, by causing them to inhale the breath of persons affected with phthisis. These isolated observations have not been corroborated by other investigators. The results of many most carefully carried out experiments have been quite negative, and the evidence against the infectivity of the breath is overwhelming.

The milk of tuberculous women, cows, or other animals has not been conclusively proved to contain bacilli or to be infective, unless the breast or udder is affected with tubercle. A large number of experiments by inoculation and feeding with the milk of tuberculous cows, free from udder disease, were made by Sidney Martin for the Royal Commission of 1890, with negative results. Recently, however, Adami in Canada, and Rabinowitsch in Berlin, have reported finding what they took to be tubercle bacilli in the milk of such cows, but they have not succeeded in proving by inoculation that the bacilli were genuine tubercle bacilli.

Bacilli outside the body. — The chief outlet for the bacilli from the human body is by means of the expectoration. A phthisical patient with active disease expectorates in the twenty-four hours thousands of millions of bacilli. Among the lower classes in England, as well as abroad, expectoration is freely deposited on the pavement and on the floors of rooms or public conveyances, or is spat into handkerchiefs, where it is allowed to dry. The dried expectoration thus becomes scattered about in the rooms where phthisical patients live, and these, together with public conveyances and places of entertainment or public worship, can hardly escape becoming foci of infection. We have seen how long dried bacilli will retain their virulence, and for the dried sputa the same is true.

A most exhaustive research on the distribution of the bacillus outside the body was made by Cornet. He experimented with dust collected in various quarters of Berlin. Intraperitoneal injections were made with this dust on 392 guinea-pigs. In 128 cases the dust communicated tuberculosis. He found it most frequently virulent in hospital wards containing phthisical patients, then in private rooms occupied by the same, and next in the galleries of lunatic asylums. The dust from the street, from surgical wards, or from private houses not occupied by consumptives, gave negative results.

More recently Straus succeeded in proving the existence of tubercle bacilli in the interior of the nasal cavity of healthy individuals frequenting places inhabited by consumptives. He found that out of twenty-nine individuals, free from the slightest suspicion of tuberculosis, nine harboured the tubercle bacillus in their nasal cavities. Of these nine, six were hospital porters whose duties were cleaning and dusting, two were hospital students, and one was a patient who had been some months in the hospital. The tubercle bacillus has, moreover, been found in the bodies and excrement of flies in apartments occupied by consumptives. It is obviously of vast importance that the expectoration of tuberculous patients should be so dealt with that its virulence may be destroyed. On this subject we shall say a few words later.

The modes of infection.—These are inoculation, inhalation, and ingestion into the alimentary tract.

Inoculation.—Villemin in 1865 first clearly demonstrated that tuberculosis was a disease inoculable in the lower animals. He took material from tuberculous lesions, and inserted it under the skin of various animals, and found that the disease was thereby reproduced in these animals. His conclusions were at the time fiercely opposed, but have now long been universally accepted and confirmed. When the bacillus was discovered, its pure cultures were immediately found to be capable of producing the disease by inoculation. One of the most certain modes of producing tuberculosis experimentally is by intraperitoneal inoculation. The guinea-pig is the most sensitive animal to such inoculations, which accordingly furnish a most conclusive method of testing whether suspected material is tuberculous or not. Inoculation, however, is a very unusual mode of infection in the human subject. The disease produced by inoculation in man is, moreover, as a rule a local one. Instances of local tubercle on the hands have been met with in the case of washerwomen, and post-mortem room porters and demonstrators; and tuberculosis has occasionally been communicated like syphilis by circumcision, in some of which cases suction of the wound by a phthisical operator has been found to be the cause. The communication of tubercle by vaccination may be said to be absolutely without proof. The cases where such has been alleged do not bear investigation. All experiments hitherto scientifically made have proved negative.

Inhalation.—Villemin also was the first to show that tuberculosis could be communicated by inhalation of dried tuberculous products, and to recognise the danger and infectivity of dried sputum from a tuberculous patient. Since his time numerous experiments have proved that the inhalation of air containing dried tuberculous expectoration will readily induce tuberculosis in even the most refractory animals. The fact that the lungs and the bronchial glands are the earliest as a rule to suffer in tuberculosis, and that they are by far the most commonly and most

widely affected, argues strongly in favour of the view that it is by means of inhalation that man most commonly becomes infected by tubercle. Experimental tuberculisation, however, has demonstrated that, in whatever way the bacilli may be introduced into the body, whether by hypodermic or intraperitoneal injection, or by the mouth, the lungs may suffer out of proportion to the rest of the body. A process of exclusion will show that in the vast majority of cases infection must come by the air.

We have seen how universal the tubercle bacillus is in the dust of rooms which have been occupied by phthisical patients. We know that the opportunity for infection by inhalation exists wherever phthisical patients have been recently, who have been careless about the disposal of their expectoration. Both theory and experiment combine to show that inhalation is by far the most common mode of infection.

Ingestion.—Whilst tuberculosis by inhalation is undoubtedly the most common mode of infection, it has been abundantly shown that tuberculosis may be communicated by food. Animals fed on tuberculous matter seldom fail to become tuberculous themselves. Different kinds of animals differ in the facility with which they are rendered tuberculous in this way. The pig is one of the animals most susceptible. The ruminants are more readily affected than the carnivora. Rabbits and guinea-pigs show little resistance. Young animals are less refractory than old.

The nature and situations of the lesions produced by ingestion are of great importance in connection with human tuberculosis. In the case of the pig the infection appears to occur at the fauces and tonsils, for the malady begins in that animal with swelling of the glands of the neck, throat, and head, and ulcerations of the pharynx and soft palate. As a rule, however, the first and most evident lesions are met with in the intestines, in Peyer's patches, and the solitary follicles. Next to the intestines, the mesenteric glands are most commonly affected, then the other lymphatic glands, etc. It must be pointed out that sometimes the intestines escape, while the mesenteric glands show infection. In man the intestines very frequently become secondarily affected, from the patient swallowing the tuberculous sputum. In children, and probably also in adults, primary intestinal or mesenteric tuberculosis occurs as the result of ingestion of tuberculous food; but, as has been said, this mode of infection is probably not nearly so common as that by the respiratory tract.

We have already referred to the prevalence of tuberculous disease among the lower animals, on which subject more is said below. The disease is particularly prevalent among cattle, and a matter of vast importance to the community is the possibility of infection through milk and meat. The experiments of many observers, among them those of Sidney Martin, show, as previously stated, that milk is usually not infective unless the udder of the cow is itself tuberculous. Where the udder is tuberculous, the milk, according to Martin, "possesses a virulence which can only be described as extraordinary. All the animals inoculated showed tuberculosis in its most rapid forms."

We have seen that the virulence of tubercle bacilli can be entirely destroyed by boiling. The public have therefore a perfect safeguard, if they choose to use it. As, however, a large quantity of milk is consumed uncooked, the greatest vigilance should be exercised, by systematic inspection of dairy cows, to prevent the delivery to the public of contaminated milk. There is no doubt that the danger is a real one, but the extent to

which infants are infected by milk has been exaggerated. The distribution of the lesions in them more frequently points, as it does in adults, to infection by the respiratory tract than by the alimentary. Tuberculosis of the bronchial glands is more common than tuberculosis of the mesenteric, and when both exist the former is usually the further advanced.

It has been shown that butter, cream, and cheese manufactured from tuberculous milk are equally infective with the milk itself. There is, however, much less risk of infection from the ingestion of these substances than there is in the case of milk, because the amount consumed at any one time is so much smaller. It is a demonstrated fact that the presence of a certain minimum number of bacilli is required in order to infect by means of food. The ingestion of a few bacilli is little likely to produce tuberculosis.

In the case of meat, the principal danger lies in contamination of the surface with tuberculous matter from the internal organs. Tubercle in the interior of the muscles is an extreme rarity. As in cooking, the exteriors of joints, steaks, etc., are exposed to sufficiently high temperatures to kill any bacilli in matter with which the surface may have been smeared, ordinarily such contamination will prove quite harmless. A real danger, however, exists when joints are prepared by rolling, so that the possibly contaminated exterior comes to occupy a central position. In such cases surface bacilli might never be exposed to a high enough temperature to destroy their virulence. As in the case of tuberculous sputum, so in the case of the tuberculous organs of an animal, precautions should be taken rapidly to destroy the infective substance, as well as to avoid contamination of the healthy parts.

Geographical and racial distribution.—As regards the geographical distribution of the disease, it may be said that wherever men are gathered together, there tuberculosis will be found. Where they lead a healthy out-of-door life, and are well housed and well fed, there tuberculosis will be rare or unknown; where the opposite conditions prevail, it will be common. In all the populous parts of Europe, Asia, Africa, America, and Australia, it flourishes, in spite of enormous differences of climate. It is useless to particularise its distribution in individual countries. The warm and moist climates are more favourable for the spread of tuberculosis than the cold and dry. The best climate in the world will have little counteracting effect where sanitation is neglected, human beings are crowded together, and the disease has once been introduced.

That *race* has little to do with the incidence of the disease, is shown by the susceptibility of peoples, free from the disease in their own homes, when placed under altered conditions. Thus the native of the Soudan frequently falls a victim to phthisis when removed to Cairo. In spite of magnificent climatic conditions, the Red Indian and the Maori both readily succumb to the disease when exposed to infection. The negro in America and in the colonised parts of Africa is very liable to it.

While latitude and longitude appear to have little to do with the prevalence or rarity of the disease, it has been maintained that *altitude* has a very important influence. It was reported that phthisis was extremely rare in the cities on the high plateaus of the Andes, such as Santa Fé de Bogota, Quito, Puebla, etc., and in the central plateau in Mexico. The rarity of tuberculosis in these towns has no doubt been considerably exaggerated. The value of the high altitudes depends on the dryness, purity, and stillness of the air, and the large amount of sunshine during the winter months. It has been shown by Bowditch in the United

States, and Sir George Buchanan in this country, that excess of moisture of the subsoil goes along with an increased prevalence of the pulmonary form of tuberculosis. Improved drainage of the subsoil is followed by diminution of the death-rate from pulmonary phthisis. It is probable that dampness of the dwelling, due to a moist subsoil, acts indirectly by setting up catarrhal conditions of the respiratory tract.

Distribution among the lower animals.—Tuberculosis is a disease to which not only man, but many domestic animals, fall victims, and its occurrence in the latter is of great interest in connection with the causation and dissemination of the malady. Wild animals are also liable to be affected by it when kept in captivity, but it is not certain that it ever affects them except under artificial conditions. The disease is capable of being inoculated in probably every member of the mammalian class. Under the names of *Pommelière, Perlsucht,* and Pearl disease, bovine tuberculosis has been known for many years as one of the most common and most fatal diseases of cattle in this and other countries.

From the records of the Copenhagen slaughter-houses, we find that, during the four years 1890–93, out of 132,294 oxen and cows, 23,305 showed evidences of tubercle, giving a proportion of 17·7 per cent. In 1893–94, 18,462 cattle were tested by means of tuberculin in Denmark in 717 farms; 7428 were found to be tuberculous, or 40·2 per cent. In Holland, in the large towns, a large and increasing proportion of cattle are found to be tuberculous. In Germany, tuberculosis of cattle appears to be equally common. From the Berlin slaughter-houses, the report of the year 1892–93 states that out of 142,874 oxen and cows, 21,603 showed evidences of tubercle, giving a proportion of 15·1 per cent.

Similar statistics are not to be had for this country, a record being kept only of the cases where the carcase has been condemned on account of tuberculosis. At Edinburgh during the four years 1887–90, out of 112,981 cattle slaughtered, 414 were condemned, on account of tuberculosis, as unfit for human food. This represents only a small proportion of the whole number affected with tuberculosis. Two striking instances of the prevalence of tuberculosis among cattle in this country may be mentioned. An investigation of 300 milch cows, slaughtered on account of an outbreak of pleuro-pneumonia, was made in Edinburgh in 1890. Of these, 120 were found to be affected with tuberculosis, or 40 per cent., and the number in different cow-houses varied from 12 to 83 per cent. The result of testing the Castlecraig herd in 1895 showed that out of forty cattle, which, with one exception, had the appearance of being healthy and vigorous, thirteen were unmistakably tuberculous, and three doubtfully so. In infected breeding and dairy herds in New York, Nunn found a maximum of 98 per cent. and a minimum of 5 per cent. tuberculous, while in healthy country districts he found hundreds of cows in adjoining herds without a trace of tuberculosis among them. Calves are much less affected with tubercle than full-grown cattle. Thus out of 185,765 calves in Copenhagen, only 369, and out of 108,248 calves in Berlin, only 125, showed evidence of tubercle.

The causes of the frequency of tuberculosis among cattle are the same as those which we find hold in the case of man—overcrowding, lack of light, want of ventilation, disregard of cleanliness, insufficient or unwholesome food, overmilking, breeding too young, and in-breeding. Where such conditions prevail, the presence of one case of *Pommelière* in a cow-house will be certain to be followed by a more or less general outbreak. The

horse and ass are only rarely affected with tuberculosis, although both can be successfully inoculated with the disease. Sheep and goats are also but rarely affected. Of 337,014 sheep at Copenhagen in 1890–93, only one, and of 355,949 at Berlin in 1892–93, only fifteen, were tuberculous, a very striking contrast to the figures for cattle. Isolated cases of tuberculosis in goats kept for milking purposes have been from time to time recorded. Both kinds of animals can be readily rendered tuberculous by feeding with tuberculous matter, or by intravenous injection of the same. In the case of swine, the prevalence of the disease holds an intermediate place between that in the case of cattle and sheep. Of 8292 swine slaughtered at Copenhagen in the years 1890–93, 1272 were tuberculous ; and of 518,073 at Berlin, in 1892–93, 7055 were affected. In 1890, at Amsterdam, out of 30,406 swine, 323 were tuberculous. There is a very great difference, then, between the statistics of different countries. Bouley suggests that the explanation is that swine affected with tuberculosis are found not to fatten, and are made away with clandestinely. However this may be, it is found that swine may be very readily rendered tuberculous by feeding with tuberculous material. Young pigs show a special proclivity to the disease. In the pig the lesions are chiefly situated in the digestive tract, which may be affected throughout its whole length.

Spontaneous tuberculosis of the dog, although rare, has been fairly frequently recorded. Eber of Dresden found, out of 400 dogs on which he made an autopsy, eleven tuberculous; and Cadiot at Alfort found forty out of 9000 dogs tuberculous. The dog appears to become infected by living with tuberculous masters, and, as a rule, it is infected through the respiratory tract. It is easier experimentally to render dogs tuberculous by causing them to inhale infected air, than by subcutaneous inoculation. Feeding experiments have hitherto not been successful. On the other hand, tuberculosis can nearly always be produced by means of large intraperitoneal or intravenous injections of mammalian tubercle bacilli. The dog has been found specially resistant to avian tubercle, even large intravenous injections producing no appreciable lesions, although a very large dose may induce a condition of marasmus terminating in death. A point of some interest is that in canine tuberculosis the liver is frequently affected with tuberculous nodules, which might easily be mistaken for cancerous growths. The cat is more frequently affected with spontaneous tubercle than is the dog, and is more readily rendered tuberculous experimentally. According to Jensen, infection appears generally to take place by way of the digestive tract. Kittens are specially susceptible.

The quadrumana in confinement are extremely frequently attacked with tubercle, which kills a large number of them. It is not known that they are ever affected by the disease in their natural condition. Campbell, out of thirty-eight monkeys examined post-mortem at the London Zoological Gardens, found tuberculous lesions in twenty, while Forbes found a proportion of 43 per cent. in 173 examinations. The pulmonary form, as in man, is much the most frequent. Nearly all classes of animals, such as lions, tigers, giraffes, bears, panthers, jaguars, etc., kept in confinement in zoological collections, have been found at one time or another to be affected with tubercle.

Although rabbits and guinea-pigs are readily rendered tuberculous experimentally, there is no satisfactory evidence that they are ever affected spontaneously, except under artificial conditions. It has been stated, however, that rabbits are frequently tuberculous, but there is

no evidence in support of this assertion; all experimenters are agreed on the absence of tuberculosis among them, except when artificially introduced. Sidney Martin states that the spontaneous occurrence of tubercle in a rabbit or guinea-pig, in a laboratory for pathological research, can only result from a breach of the strict hygienic rules which are a *sine quâ non* of such an establishment. He made 597 post-mortem examinations on guinea-pigs. In not one of the non-experimental animals, 203 in number, was a tuberculous lesion discovered, and tuberculosis was found only in those of the experimental animals which were inoculated or fed with tuberculous material.

Rats and mice are less susceptible to tuberculosis than rabbits and guinea-pigs; and certain varieties, such as white mice, white rats, and the Algerian rat, show a considerable degree of resistance to experimental inoculation. Birds are liable to be affected with a form of tuberculosis, but there is reason to believe that this differs essentially from the ordinary disease which we are considering. It has been already pointed out that, while the morphology of the mammalian and avian bacilli is practically the same, there are distinct differences in the vegetability; and the appearances of the cultures are such as to enable skilled observers at once to discriminate between them.

Even more striking are the differences in the inoculability of the two forms of tubercle. Although a number of cases have been reported where fowls have been said to have become infected with tuberculosis through feeding on tuberculous sputum, such cases do not bear investigation, and are altogether contrary to what has been observed by scientific experiment. Straus and Wurtz systematically fed eight fowls with tuberculous sputum for months without succeeding in infecting them. Nocard equally failed in feeding experiments. Inoculation experiments on birds have only very rarely succeeded with mammalian tubercle, while with avian success is the rule. The dog, as has been pointed out, has proved absolutely refractory to avian tubercle, while it is fairly readily inoculable with mammalian, provided the dose is a large one. In the guinea-pig, the inoculation of the avian bacillus scarcely ever produces an eruption of tubercles, while inoculation with the mammalian does so invariably.

Until it has been conclusively shown that the mammalian tubercle bacillus can be transformed into the avian, and *vice versâ*, the two must be regarded as distinct, although presenting many resemblances. Some ingenious experiments recently made by Nocard go some way to show that this can be done. He introduced collodium sacs, filled with bouillon cultures of human tubercle bacilli, into the peritoneal cavities of fowls. After some months the fowls were killed and the sacs removed. After several passages it was found that the bacilli were so altered as to give rise to what appeared to be avian tuberculosis.

In birds, the digestive organs are the principal seats of tuberculous lesions. The liver is usually the organ which is most extensively affected. It becomes crowded with tubercles, varying in size from a millet seed to a walnut. Histologically, avian tubercle closely resembles mammalian. Giant cells, though sometimes absent, are not infrequently present. Bacilli are often found in extraordinary abundance.

It has been estimated that about 10 per cent. of farmyard poultry are affected with tuberculosis. The common fowl, turkeys, pigeons, and pheasants are all very liable to it. Ducks and geese, however, are seldom affected, and even when much exposed to the contagion, remain immune.

Parrots are frequently attacked, and in them there is the peculiarity that the skin not uncommonly shows tuberculous lesions, especially about the head. In the case of parrots, it has been maintained that the disease is communicated by mouth-feeding, etc., from the human subject; and Straus and others have recently brought forward evidence showing that the parrot may be affected by mammalian as well as by avian tubercle.

A form of tuberculous disease of fish has been described by Dubard. The animals affected were carp, which lived in a pond that had been contaminated with tuberculous matter from a phthisical patient. Cultures from the tumours yielded bacilli varying little from the mammalian type. They could, however, be grown at the ordinary temperature on all the usual media, and filamentous and dichotomous forms were not uncommon. The cultures were not pathogenic to warm-blooded animals. The observations of Sibley in regard to spontaneous and experimental tuberculosis in snakes require confirmation. In the case of the frog, experimental inoculation has failed, although the presence of the bacilli in the organs of the animal has been shown by the reproduction of tuberculosis in guinea-pigs, by inoculation with fragments of these organs.

Experiments have been made to show that earth-worms may form vehicles for the tubercle bacillus. Tuberculous matter was mixed with the earth in which the worms were confined. After a few weeks both the tissues of the worms and the contents of their intestines were found to be capable of producing tuberculosis on inoculation. These experiments also require confirmation.

Morbid anatomy.—**Miliary tubercle.**—*Macroscopic appearances.*— The miliary tubercle, when seen with the naked eye, or by the aid of a magnifying glass, appears as a little round granule. It varies in diameter from 0·05 mm. to 2 or 3 mm. When recent it is translucent, of a greyish white colour, but soon becomes opaque and yellowish at the centre. It is often surrounded by a reddish vascular zone. It may be, however, impossible to distinguish with the naked eye early tubercles from the tissues in which they are embedded.

Histology—When a section of an early tubercle is examined under the microscope, it is seen to consist of a group of round cells arranged about a centre, at which are situated one or more large multinucleated cells—the so-called giant cells. No blood vessels are present in the nodule. At a later stage the centre of the tubercle will be found to have become caseous, to have no definite structure, and to stain feebly or not at all. The various elements are embedded in a ground substance of soft protoplasm, which sometimes takes on a fibrillated or reticulated appearance.

We shall consider first the giant cell. The giant cell is a body with a long diameter of from ·05 mm. to ·2 or ·3 mm., of irregular shape, and consisting of granular protoplasm, containing twelve to twenty or thirty nuclei, which are generally ranged along the margin or collected towards one extremity. It has various branching peripheral processes. Its nuclei stain deeply, and it is thus well distinguished from the other cells. A tubercle may contain several of these bodies. Surrounding the giant cell or cells is a zone formed of epithelioid cells. The epithelioid cells are rounded or flattened bodies, slightly larger than leucocytes, with granular protoplasm, containing one or more oval vesicular nuclei, which stain feebly. The epithelioid cells may be grouped only in close proximity to the giant cell, or they may reach quite to the periphery of the tubercle.

Finally, there is a zone consisting of small round cells, with single relatively large nuclei which stain readily. These have been called embryonic or lymphatic. They are usually closely set.

Retrograde changes.—A characteristic feature of the tubercle is the absence or obliteration of vessels. In association with this we find the central parts of the tubercle undergo a transformation, consisting in caseous degeneration. This degeneration results in the fusion of the cellular elements and their infiltration by fatty granules. It commences at the centre of the tubercle in the giant cell, and gradually spreads to the periphery. The tubercle then becomes opaque and yellowish, and the details of its structure quite obscure, and it is no longer capable of being coloured by staining reagents. Later, the caseous matter may soften, and if there is an outlet for this softened material, as in the case of the lung, kidney, or intestine, it may be eliminated. With or without softening, caseous matter may undergo another change, becoming calcified from deposition of lime salts, principally the phosphate. Calcification is a frequent change in old tubercle in cattle and swine as well as in man. It occurs also in avian tuberculosis. It has not been observed in guinea-pigs or rabbits. Instead of undergoing caseation, tubercles are sometimes converted into fibrous tissue. They then form little hard nodules, formed of homogeneous fibrous tissue, containing scanty small round cells, and are generally devoid of vessels. This change is less frequent than the caseous. The caseous tubercle is one which has died young. The fibrous is one which has grown slowly, and has passed into this condition without caseating. Sometimes the two processes are combined, the central part caseating while the peripheral becomes fibrous. The caseous material then becomes encysted, and may later become calcareous. The fibrous change is frequently accompanied by pigmentation.

Confluent tubercle, the tuberculous infiltration of Laennec.—In association with the bodies just described are often seen larger grey or yellow caseous masses, either in the lung or glands or elsewhere. The essential identity of these masses with the miliary tubercle was maintained by Laennec, and although this was denied by Virchow, and disputed by many pathologists, it has now been thoroughly established, and both have been shown to be dependent on the presence of the tubercle bacillus. The larger masses in most cases result simply from the coalescence of a number of closely-set miliary tubercles, each of which has undergone caseous degeneration, and unites to form a caseous whole, in which it is impossible to recognise the individual tubercles. On a smaller scale, this coalescence takes place even in the case of the bodies which, from their size, may be called miliary, the larger of these being always formed by the fusion of several smaller.

Some maintain that the larger masses always arise in the manner just described, but it is not possible to give a satisfactory demonstration of this; and it seems very probable that without formation of actual miliary tubercles, with or without giant cells, a diffuse tuberculous process, characterised by a small-celled growth, consisting of epithelioid and small cells, may arise. Such a small-celled growth, at any rate, is frequently found in the lungs, infiltrating the bronchial sheaths and the alveolar walls, and accompanied by a similar growth in the alveoli and in the lumina of the bronchi. That this is really tuberculous and essentially the same as the miliary tubercle, although differing from it in form, is shown by its passing through the same transformations as the latter does, and by its constant

association with the tubercle bacillus. The tuberculous infiltration may caseate, and the necrosed tissue may soften, separating and being discharged at the surface of the mucous membranes, or forming an abscess where there is no outlet; or it may undergo the fibroid transformation; or, as in the case of the miliary tubercle, both these processes may be combined. Tubercle in either of the two forms just mentioned may be, and frequently is, associated with simple inflammatory processes.

Relations of tuberculous lesions to bacilli and other micro-organisms.—We have hitherto said nothing as to the exact relation of the bacillus to the tubercle. There is nothing absolutely diagnostic of tubercle in its anatomy. Certainty as to the nature of a suspected lesion can be established only by the discovery in it of the tubercle bacillus. Bacilli are to be found most certainly in young and growing tubercles, where the latter are beginning or rapidly developing. One or two bacilli appear outside the nucleus in the interior of the epithelioid cells. At a later stage they increase in number, occasionally filling the whole cell. It is, however, in the giant cells that the presence and distribution of the bacilli are most characteristic and interesting. The number of bacilli seems to be in inverse proportion to the number of giant cells. Where these are abundant the bacilli are few, where scanty the bacilli are numerous.

In the case of slowly-growing tubercles, the bacilli are in general few, and are met with almost exclusively in the giant cells, and there in very small number. When the growth is more rapid, the number of bacilli contained in the giant cells becomes very large, and may exceed fifty. In suitably stained sections they may be seen, under a comparatively low power, forming tiny red or blue rings within the circle formed by the nuclei. When the bacilli are few, they generally occupy a position either at the centre or at the pole opposite to the nuclei. At the commencement of caseation, especially when the process is rapid, the bacilli are still visible in large number. Later, they cease to fix the colouring reagent. Nevertheless in caseous centres there exist modified forms of the bacilli which, although impossible to stain, are virulent and capable of growth and reproduction.

It is chiefly to the researches of Baumgarten that we are indebted for a knowledge of the histogenesis of tubercle. He has shown that the presence of the bacilli in the tissues is followed by karyokinesis of the fixed cells, the connective tissue cells, the endothelial cells, or the epithelial cells, as the case may be. The cells which undergo karyokinesis may contain one or more bacilli, but in most cases the bacilli are near but not included in the cells. All the stages of transformation of the fixed cells into epithelioid cells can be witnessed. The early tubercles almost exclusively consist of such epithelioid cells derived from the fixed cells. A little later, leucocytes make their appearance, derived by diapedesis from the neighbouring vessels. These, however, do not undergo such modifications as division of nuclei and increase of protoplasm, but rather shrivel up, and later break up into small granules. In some cases the invasion of leucocytes may be so rapid and active that the tubercle may assume the appearance of a group of leucocytes. When the process is slower, the leucocytes may be almost entirely absent, and the tubercle then remains composed almost entirely of epithelioid cells. It is the presence of the leucocytes which determines the caseous degeneration. The giant cells result from the proliferation of the nuclei of the epithelioid cells, of which the protoplasm increases but shows no tendency to division. Baumgarten supposes

that for the production of giant cells a more feeble degree of irritation is required, and that, when the irritant is intense, cellular division becomes complete, with the result that only epithelioid cells are met with in the tubercle. Thus, in acute miliary tubercle, where the bacilli are abundant, the giant cells are few; in lupus, where they are few, the giant cells are numerous.

The conclusion is that the epithelioid cells and the giant cells are derived by karyokinesis from the fixed cells of the tissues, and while migrating cells escape from the inflamed vessels in the neighbourhood and invade the tuberculous nodule, these last are not capable of further evolution, give birth neither to epithelioid nor giant cells, but rapidly undergo the ordinary changes of disintegration.

Metchnikoff's views, which are not generally accepted, are that the epithelioid, as well as the giant cells, are phagocytes of mesodermic origin; and that the giant cells, far from being elements struck with partial necrosis, are, on the contrary, particularly living, and constitute the essential defence of the organism against the parasite of tuberculosis.

Other micro-organisms.—Of late years a good deal of attention has been directed to other micro-organisms which have been found associated with the tubercle bacillus in tuberculous lesions. It has almost seemed as if the unity which had been restored by the discovery of Koch was once more to be disturbed and duality re-established.

It is principally in connection with the lesions in chronic pulmonary tuberculosis that these microbes have been found, but they have also been observed in the acute form. The micrococci which are chiefly found are the pneumococcus and the microbes of suppuration, the *Streptococcus pyogenes* and the *Staphylococcus aureus*. Sputa washed in sterilised water, to free them from micro-organisms derived from the upper air passages, sometimes contain only tubercle bacilli, but at other times streptococci, etc., are found. Some have thought that the broncho-pneumonic lesions are always, in the first place, due to these micro-organisms, and that the tubercle bacillus comes secondarily and causes the caseation. The hectic fever of phthisis has been attributed to the invasion of the blood by these microbes rather than to the action of the tubercle bacillus and its toxines. Most careful examinations of the blood by Straus have failed to discover the presence of any such micrococci during the hectic fever.

It seems probable that the presence of micrococci in the affected parts is an accidental and secondary phenomenon. This is supported by the facts, first, that their presence is by no means constant in pneumonic areas; and, second, that intratracheal injections of pure cultures of the tubercle bacillus will induce exactly similar lesions in which no other microbes can be found.

Serum diagnosis.—A brief reference may be made to the recent endeavours of Arloing and Courmont to apply the method of serum diagnosis to tuberculosis. For this purpose it was first necessary to produce a culture in which the bacilli should be homogeneously distributed, a matter of great difficulty. A culture in glycerin peptone bouillon was produced by inoculation with a bacillus much attenuated by long cultivation in the laboratory. To secure homogeneity, the culture was daily shaken. Re-inoculations were made once a month, the same culture medium and the same amount of mother culture being used. The cultures thus obtained showed marked changes; the bacilli became almost entirely isolated, causing cloudiness of the medium, and

their cultural properties proved to be greatly altered. Motility becomes a marked feature of the liquid cultures. When homogeneous cultures thus prepared were used, it was found that normal blood serum produced no agglutination in greater dilution than 1 in 5, and only occasionally then. In tuberculous cases, agglutination occurred in dilutions of from 1 in 5 to 1 in 20, the most marked reaction being observed in cases where the lesions were limited and discrete, and negative results occurring where the disease was widely spread. The great difficulties which have attended the production of homogeneous cultures have prevented a trial of the method on a sufficiently extensive scale to establish how far dependence can be placed on the results, but it is evidently a method which may prove to be of great value in the diagnosis of early tuberculosis.

ACUTE MILIARY TUBERCULOSIS.

Etiology.—By far the larger number of cases of acute miliary tuberculosis occur in early childhood, but in later life it is between the ages of 20 and 30 that it is most frequently met with. The disease is usually secondary, occurring for the most part in connection with chronic tuberculosis of the bronchial, mesenteric, or other glands, or of the vertebræ or other bones. Alcoholic subjects appear to be specially liable to acute miliary tuberculosis. Occasionally the disease occurs in an epidemic form. It is evident from the distribution of the lesions that the virus has been carried to the various parts of the body through the blood stream.

Morbid anatomy.—In acute miliary tuberculosis tubercle appears in nearly every organ in the body. The lungs hardly ever escape, although the extent to which they are affected varies greatly in different cases. There may be only a sparse deposit of tubercle, scarcely visible to the naked eye, or there may be a very general tuberculous infiltration.

We shall first describe the pulmonary form of acute miliary tuberculosis. In this, little grey nodules, just visible to the naked eye, are thickly distributed throughout the lungs. They are often universally diffused, but may be irregularly grouped, possibly being more numerous in the lower lobes. They are generally thickly distributed underneath the pleura. Usually they are discrete, but they may be confluent or arranged into racemose clusters. Often they can be more readily felt than seen, being hard to the touch. They may be surrounded by a zone of hyperæmia and pigmentation. A few of these nodules may be seen on section to be opaque in the centre, forming a transition to another kind of granulation almost as common. These are somewhat larger and softer, whitish in colour, opaque and yellowish at the centre or yellow throughout. They may occur in racemose groups the size of a currant or raisin. They may soften and form small abscesses and cavities. Such abscesses may undermine and perforate the pleura and cause pneumothorax, but this is very uncommon. The lungs containing these granulations are usually congested and redder than normal, and are often emphysematous. Here and there are patches of collapse, or larger or smaller areas of consolidation, principally in the lower lobes and posterior borders. Three forms of consolidation are met with, first ordinary red hepatisation, in which, however, tubercles may be found under the microscope; second, tracts of grey, semi-transparent exudation; and third, infiltration of a uniform yellow colour, at the edges of which fine yellow or white granulations may be detected.

When sections of the lung are examined, after hardening and staining

in the usual way, it is found that the grey miliary nodules consist of groups of alveoli filled with round cells. The elastic fibres of the alveolar walls can be seen, but their capillaries can no longer be made out. The round cells are granular, and contain nuclei which do not stain readily. They are in close apposition to one another. The bronchioles, leading to the alveoli, are also filled with a similar exudation, but besides this there is a diffuse thickening of their walls. This thickening has the structure of ordinary tubercle, such as already described. Sometimes it entirely surrounds the bronchus, sometimes is only situated on one side so as to form a crescent. It is generally found at the terminal bifurcation of the intra-lobular bronchus. Similar structures may be seated on the walls of the minute branches of the pulmonary artery. The tubercle of the lung is thus composed of tubercle proper, together with the exudation into the interior of the pulmonary alveoli and bronchioles.

An important question is whether the exudation in the alveoli differs at all from the ordinary exudation of pneumonia.

We have seen that the bacilli first cause a karyokinesis of the fixed cells of the tissue, and that later there is an invasion of round cells which escape from the surrounding vessels. The filling of the alveoli with such products cannot be considered as in any way different from that of pneumonia. It must be remembered, however, that in pneumonia the walls of the alveoli undergo little change, the capillaries are uniformly distended, and the exudation may be easily separated. We find, on the other hand, in the case of the pulmonary tubercle, that the capillary vessels early become obliterated, this obliteration being a constant feature, and the exudation cannot be removed without difficulty. We have already referred to the presence of other micro-organisms besides the tubercle bacillus in these broncho-pneumonic areas, and stated that we believed their occurrence to be accidental and secondary.

The serous membranes may be generally or individually affected. There may be effusions of serum in the cavities or a deposit of sero-fibrinous exudation lining the membranes, while tubercles may be very closely set over the whole surface. For descriptions of these changes and of tubercle of the intestines, reference must be made to the special sections treating of the same.

When tuberculous meningitis is present, it will be observed that the surface of the brain is injected, and rather dry and sticky, while the convolutions are somewhat flattened. On removing the brain, there is probably a considerable escape of cerebro-spinal fluid. There is an effusion of inflammatory lymph, which as a rule is limited to the base, and covers the chiasma and under surface of the pons and medulla. The Sylvian fissures are glued together, and cannot be separated without tearing the cerebral tissue. Tubercles can often be seen along the various branches from the circle of Willis, especially along the middle and posterior cerebral arteries, and are best seen by floating out these arteries and their branches in water. Sometimes the microscope is required to detect the presence of tubercles. Sometimes the meningeal tubercles accompanying meningitis may be larger, attaining the size of a hemp seed, and in such cases they may be fibrous and obsolescent, showing that they are of considerably older standing than the meningitis. The lateral ventricles are frequently distended with fluid, and their floors are softened, while tubercles may be found on the velum interpositum and choroid plexuses.

The lymphatic glands are very frequently affected. One or more of the bronchial glands are enlarged and caseous, and a similar condition is often found in the mesenteric glands. The liver almost always contains miliary tubercles. A few are generally to be seen beneath the capsule, but often they require the microscope for their detection. The spleen likewise is usually affected, being enlarged, and containing tubercles which may be grey or yellow, and of varying size. In the kidneys a few tubercles can usually be seen on the surface after stripping off the capsule. Tubercle has been found in practically every organ, although less frequently in others than in those mentioned. Tuberculous phlebitis and endarteritis are not uncommon, and will be referred to under the heading " Tuberculosis of the Vascular System."

Symptoms.—The symptoms of acute miliary tuberculosis vary in different cases, according as the stress of the disease falls on one part of the body or another. Four forms may be described, in which most cases can be included. These are a latent form, an abdominal or typhoid form, a pulmonary form, and a cerebral form. Certain symptoms which are common to all the varieties may first be mentioned. Among these are pyrexia, prostration, rapidity of pulse, and cyanosis.

Fever, the most striking feature of which is its irregularity, is more or less constantly present. It may be continuous, with but little difference between the morning and evening temperatures; or remittent, resembling that of enteric fever; or intermittent. Continuous fever, with differences between the morning and evening temperatures of less than 2° F., is the type which has been most frequently met with at the Brompton Hospital. In the remittent type, the afternoon or evening temperature is, as a rule, higher than the morning. Remissions of 3° F. are not uncommon, both the morning and evening temperatures being pyrexial. Less commonly the remissions may amount to 5° or 6° F., the lower temperature being normal or subnormal, the remittent type then becoming the intermittent. The remissions may be attended by profuse perspirations. In most cases the remissions and exacerbations are very irregular. Although the remissions are usual in the morning and the exacerbations in the afternoon, an inverse type is sometimes met with, where the temperature is higher in the morning. This inverse type is specially characteristic of acute miliary tuberculosis. In some cases considerable rises mark fresh outbreaks of tubercle. Rarely cases occur where there is little or no rise of temperature. In the meningeal form of acute miliary tuberculosis, absence of fever is not very exceptional, especially in the case of adults.

Prostration is a frequent accompaniment of all forms of acute miliary tuberculosis, but is most common with the cerebral form. It is often out of proportion to the actual strength of the patient.

Rapidity of pulse is the rule, the acceleration being sometimes very great. In exceptional cases the pulse rate is little above normal. Sometimes retardation occurs with the onset of cerebral symptoms.

A certain degree of cyanosis is often to be noticed. It points to involvement of the lungs, and accordingly is most marked in the pulmonary form of the disease. The skin is usually moist with perspiration, and an eruption of sudamina often appears on the chest. The *taches cérébrales,* wheal-like marks, readily produced by drawing the finger-nail or the point of a pencil across the skin of the chest or abdomen, although not peculiar to this disease, may very often be observed, especially in the cerebral form.

Epistaxis occasionally occurs either at the onset or at a later period. More rarely hæmoptysis ushers in the disease, and sometimes purpuric hæmorrhages appear on the skin, and bleeding occurs from the gums and into the serous cavities and joints. Emaciation is not common except in protracted cases and in the cerebral form of the disease. Among other symptoms occasionally present in all forms of acute tuberculosis are severe muscular pains.

Choroidal tubercles may sometimes be detected by ophthalmoscopic examination in acute miliary tuberculosis. They are generally most abundant near the *macula lutea*, and are often situated about the retinal vessels, which can be seen coursing over them. Their appearance is that of white round patches with soft edges. Their diameters vary from little more than that of a retinal vein to more than half that of the optic disc. They vary in number from one or two to twenty or thirty in each fundus. During the progress of the case the growth and increase in number of the tubercles may be observed. Their presence is, as a rule, unaccompanied by other choroidal changes.

We shall now consider the various forms which the disease may assume.

The latent form.—In this the symptoms do not specially point to the involvement of any particular organ of the body. It is seldom that any case remains latent throughout, but the distinctive features may be masked, and the symptoms be vague and indefinite until a late period of the disease.

In the abdominal or typhoid form the symptoms closely resemble those of enteric fever, for which the malady is usually for a time mistaken. The illness sets in gradually with weakness, fever, anorexia, and general malaise. The fever, as already described, differs from that of enteric fever by its irregularity and variations. There are, as a rule, complete loss of appetite and great thirst. The tongue is usually coated, and later becomes dry. Occasionally there is vomiting. Constipation is the rule, less commonly there is diarrhœa. Peritonitis is frequent, but seldom gives rise to very acute symptoms. The patient probably complains of pain in the abdomen, and the latter is tender to the touch. The pain is seldom severe. The abdomen as a rule is distended, and often assumes a globular shape, but it may be retracted. Sometimes, but not commonly, ascites is present. The spleen is usually slightly enlarged, but is not so likely to be felt on palpation as in enteric fever. The pulmonary symptoms are slight, and only such as result from a moderate degree of bronchitis. Acute delirium is uncommon, but torpor and mental dulness are usual. The illness is generally of longer duration in this form of the disease than in the pulmonary or cerebral types, and may last for six weeks or two months.

The pulmonary form is characterised by dyspnœa, hurried respiration, cough, cyanosis, and the symptoms generally of diffuse bronchitis.

The disease in this form usually commences with the sudden onset of acute symptoms. The respiration is always hurried, and dyspnœa is a very striking feature. Sometimes the quickening of the breathing occurs without dyspnœa being marked, but more commonly the two go together. When the difficulty of breathing amounts to orthopnœa, as is not infrequent, it is very distressing to the patient. Ordinarily the number of respirations in the minute is between thirty-six and fifty, but a rate of sixty or seventy, or in children even ninety to the minute, has been observed. Cough is

seldom absent, although it may be little troublesome. In about a quarter of the cases expectoration is absent. When present, expectoration is usually mucoid, but it may be muco-purulent. It is as a rule of moderate amount; rarely it is profuse; occasionally it is rusty or blood-stained. A high degree of cyanosis is frequently to be observed. The lips, cheeks, and finger-nails are bluish, and the extremities readily become cold. Hæmoptysis, although rarer than the other symptoms, is not very uncommon in this pulmonary form of the disease. It is more likely to occur where there has been pre-existing phthisis. The physical signs are those of bronchitis and emphysema. The lungs generally are over-resonant. The breath sounds may be weak, or harsh, or uneven. Rhonchi, sibilant and sonorous, together with medium crepitations, are generally audible over both lungs. Rarely there are patches of consolidation large enough to give rise to the usual physical signs.

The **cerebral or meningeal form** of acute tuberculosis presents the most characteristic symptoms. The illness, which is sometimes preceded by premonitory symptoms, has been divided for descriptive purposes into three stages—A stage of excitement and nervous irritation; a stage of depression; and a stage of coma and convulsions.

In the premonitory period, the patient becomes irritable, fretful, and wakeful at night. Symptoms of the pronounced disease, such as emaciation, headache, vomiting, disorder of the bowels, slowness and irregularity of pulse, giddiness, squinting, or drowsiness, may occasionally be met with.

The first stage either sets in quite suddenly with a fit, or more gradually with fever, headache, vomiting, and general irritability. The fever is of one of the types already described, but the temperature is seldom high. The pain in the head is usually very severe and paroxysmal, so that the patient screams out with it. It is often referred to the frontal region. Although almost a constant symptom in children, it is frequently absent in adults. Along with the headache there may be pain in the back of the neck and general tenderness of the scalp. Vomiting occurs at irregular intervals. The bowels are constipated. Irritability and fretfulness become more marked, and there is hyperæsthesia of all the senses. The sleep is usually disturbed, and there may be some delirium at night. Squinting or double vision, and rapidity alternating with slowness of pulse, are significant symptoms sometimes met with in this stage.

The onset of the second stage, or the stage of depression, frequently excites delusive hopes of improvement. The fever somewhat abates, or the temperature may even become normal. Irritability is replaced by apathy. The vomiting ceases. Sleep becomes almost incessant, but the patient can be roused to take nourishment or to put out the tongue. The breathing becomes irregular, and often assumes the Cheyne-Stokes character. The patient, during this stage of drowsiness, dulness, and stupor, probably on account of the persistence of the headache, sometimes utters a sharp, loud, plaintive cry—the so-called hydrocephalic cry. The head is usually retracted. Sudden flushing of the face is frequently to be observed. The *tache cérébrale*, already described, may generally be readily produced. The abdomen almost invariably becomes retracted or boat-shaped, and the body generally rapidly emaciates. Ptosis, strabismus, double vision, immobility of pupil or of eyeball, or facial or hypoglossal paralysis, may come on during this stage.

The third stage is that of convulsions and coma, or of coma alone. The temperature, as a rule, rises higher than in the second stage, but, on the whole, presents great irregularity. The coma becomes profound, and it is impossible to rouse the patient out of it. He rolls his head from side to side, tosses his hands and arms restlessly about, picks at the bedclothes, and from time to time may utter the characteristic cry. Convulsions are frequent, but vary in intensity and extent, and may be altogether absent. The pupils are dilated, unequal, and react little if at all to light.

Paralysis develops, or, if previously present, now becomes more pronounced. It generally affects some of the muscles supplied by the cranial nerves, as already mentioned, or more rarely assumes a hemiplegic form. There is usually loss of control over the sphincters. Rigidity of the limbs on one or both sides is often present, together with Kernig's sign, the inability to passively extend the legs when the thighs are flexed at a right angle. The pulse is now generally quick and feeble, although sometimes it is below the normal rate. Optic neuritis usually occurs, but is seldom intense, although it gradually becomes more marked as the illness progresses. Choroidal tubercles are less frequently observed when optic neuritis is present than when it is absent, and, on the whole, are less common in meningeal than in other forms of miliary tuberculosis. The usual duration of the illness is about three weeks. It may be added that, in the case of adults, prodromal symptoms are rarely observed, a sudden invasion with vomiting or convulsions is uncommon; emaciation is seldom a marked feature, and headache, as already mentioned, may be absent.

Diagnosis.—The diseases with which acute miliary tuberculosis is most frequently confused are acute bronchitis, broncho-pneumonia, pneumonia, enteric fever, and acute non-tuberculous meningitis.

The pulmonary form may be mistaken for acute bronchitis. In tuberculosis there is, as a rule, more marked constitutional disturbance. Dyspnœa and cyanosis are out of proportion to the physical signs. The limitation of râles to one lung, or their rapid dissemination throughout both, the onset with hæmoptysis or the presence of rusty sputa, and the existence of enlargement of the spleen, will point to tuberculosis. The character of the pyrexia may help, but this cannot be depended on. An "inverse type," if present, is, as has been said, specially suggestive of tuberculosis. If there is expectoration, bacilli should be looked for, but often none are to be found. An ophthalmoscopic examination should be made for choroidal tubercle.

Certain cases of acute pneumonia, where the cerebral symptoms are out of proportion to the pulmonary, are more likely to be mistaken for tuberculosis than the reverse. The doubt is not likely to exist for long. The sudden onset, the existence of pain in the side, the character of the pyrexia, and, above all, the physical signs and course of the disease, will generally decide. Henoch is inclined to believe that many of the cases of recovery from meningitis, especially from tuberculous meningitis, have been nothing but cases of pneumonia with cerebral symptoms which were wrongly diagnosed. In tuberculous meningitis, headache persists when delirium comes on, whereas in general diseases it ceases with the onset of delirium.

Broncho-pneumonia may be very difficult to distinguish from acute pulmonary tuberculisation. The sequence of the former affection after measles or whooping-cough may help. The rapid appearance of signs of consolidation points to broncho-pneumonia. Fixity of the râles and a

want of proportion between the dyspnœa and the physical signs are in favour of tuberculosis.

The greatest difficulty has existed in the past in distinguishing between acute miliary tuberculosis and enteric fever. The method of serum diagnosis should be applied in all cases of doubt, and will often help to clear up the diagnosis. In differentiating between tuberculous and non-tuberculous meningitis, we have specially to consider whether there exists any cause sufficient to account for the latter form.

An important aid in the diagnosis of all forms is evidence of the presence of old or recent foci of tubercle. Unfortunately, such evidence is not often available.

Prognosis.—When the diagnosis of acute miliary tuberculosis is certainly established, there is practically no hope. A few cases have been recorded where recovery has occurred from meningitis, which there has been every reason to believe was tuberculous, but they are so few that they can at the most only excite a shadow of doubt as to the result in the mind of the physician. I have never seen an acute case recover where I have found choroidal tubercle, but I have seen a patient recover in whom all the usual symptoms including optic neuritis were present. A similar case has been recorded by Samuel West. The recovery in the latter was very slow, being incomplete at the end of nine months. During the child's illness a brother died of tuberculous meningitis.

Treatment.—In acute miliary tuberculosis, treatment can only be symptomatic. If there is constipation, as is frequently the case, calomel is useful. If there is restlessness and pain, opium and bromide of potassium in small doses may be given with advantage. If there is distressing dyspnœa, the inhalation of oxygen will often greatly relieve. If the temperature is high, sponging with tepid or cold water, cradling, and other modes of reducing fever, may be employed. In tuberculous meningitis, special measures may be adopted, such as the application of cold to the head by means of an ice-bag or otherwise, counter irritation by means of blisters or mustard plasters applied to the scalp or neck, and the administration of mercury, preferably by inunction.

A case of recovery after diagnostic puncture of the spinal canal in the lumbar region has been recorded by Freyhan. In this case, 60 c.c. of slightly turbid pale serous fluid spurted out, in the sediment of which fluid pus corpuscles and tubercle bacilli were found. The patient rapidly improved after the puncture, and in three weeks was able to leave bed. In cases under my own care, I have seen only temporary if any relief from this measure. Tapping the lateral ventricles has also been tried by myself as well as others, but has failed to relieve.

TUBERCULOSIS OF THE ALIMENTARY SYSTEM.

MOUTH AND TONGUE.

Morbid anatomy.—Tuberculous ulcers are very rarely found on the lips and gums. The fact of their possible occurrence only need be mentioned. Tuberculous disease of the tongue is of more importance, and is more likely to come under the observation of the practitioner. It occurs more frequently in men than in women. The primary form is extremely rare; the secondary, much the more common, is nearly always met with in association with tuberculosis of the lungs. Four cases of secondary tuber-

culous ulceration of tongue were observed among 531 fatal cases of phthisis at the Brompton Hospital. The most likely situation for it is at or near the tip, but any part may be affected. The disease starts in the mucosa, where one or more granulations appear, and perhaps slightly project above the surface

Symptoms.—One or more of these become caseous, and an irregularly shaped ulcer forms, which gradually increases in size and depth. The floor of the ulcer is usually uneven and granulated, of a palish pink colour, and often coated with yellowish grey mucus. The edges are probably a little redder than the surrounding part of the tongue. They are generally sharply cut, but may be bevelled, as a rule are little indurated or raised, and are seldom everted or undermined. In the neighbouring portions, which are not uncommonly swollen, there are often little tuberculous nodules of the size of a pin's head, of a pinkish colour, and hard to the touch, and sometimes little yellowish grey points even tinier, and not raised above the surface. These latter are very characteristic when they exist. Scrapings of the floor may show tubercle bacilli. The submaxillary and submental glands are usually but not always enlarged. The ulcers are sometimes multiple. Occasionally the ulceration is very extensive, as in two cases reported by Morton, where ulceration extended from the frenum to the tip on the under surface. Sometimes much destruction of tissue is produced, as in a case reported by Hale White, where the anterior third of the tongue had been destroyed by ulceration. At first the sore is indolent, and pain and tenderness are absent, though both are present later.

Diagnosis.—The difficulties of diagnosis are in connection with cancer and syphilis. As regards the sore of tertiary syphilis, this is more often median than lateral. There is more tumour formation, the floor is deeper, and the edges are undermined. The lymphatic glands as a rule are not affected. Fournier discusses at great length the diagnosis from primary chancre of the tongue. The latter may affect any part of the tongue, but is unlikely on the under surface. The sore is indurated, and the glands are enlarged. The absence of induration and the presence of nodules or yellow points in the surrounding tissue, in the case of the tuberculous sore, are very important distinguishing features. The latter may also assist in distinguishing tubercle from epithelioma, which presents great difficulty, for they have the same seat, both frequently succeed injury, and the glands may be affected in both. The age may help in forming an opinion. The examination of scrapings of the floor may clear up the diagnosis. Evidence of tuberculous disease in the lung or elsewhere must be carefully sought for.

Prognosis and treatment.—The disease is usually fatal in a few months, or at longest in from one to two years. The lesion progresses slowly, and sometimes seems to be temporarily arrested or to undergo healing, but the disease invariably breaks out again. If primary, the diseased tissue should be freely removed; and if secondary, limited and small, Butlin considers removal still gives the patient the best chance. If operation is not considered advisable, non-irritating applications should be used, such as borax and chlorate of potash. Cocaine may be used to relieve pain. After cleaning and drying the ulcer, one may dust it with a powder containing iodoform 1 part, borax 3 parts, and morphine one-sixth part.

PHARYNX AND TONSILS.

Tubercle sometimes also attacks the soft and hard palate. Greyish granulations first appear, soon succeeded by ulcers having yellowish floors and slightly raised edges with tubercles on the margins. There is usually a general swelling of the parts affected.

Tubercle of the palate, like that of the tongue, is nearly always secondary to lung disease; but sometimes, when the patient is first seen, there may be no evidence of this, as in a case I had the opportunity of observing almost from its beginning. At first there was a small centrally situated ulcer on the roof of the mouth, with a caseous floor, and discharging a small amount of pus. There were no tubercles to be seen. Other ulcers soon developed, until the surface of the hard palate became almost covered with deep ulcers having nodular floors and caseating centres. Scrapings from the ulcers showed the presence of tubercle bacilli. Later there was unmistakable evidence of tubercle at the apex of the right lung. Laryngoscopic examination showed several tubercles on the epiglottis.

The tonsils also are sometimes tuberculous. In general tuberculosis, there may be a number of grey miliary tubercles in the superficial layers of the mucosa, or situated more deeply in the reticulated follicular tissue. In the chronic type the superficial tubercles become caseous, forming opaque yellowish projections, which soon ulcerate. Tubercles deeply situated coalesce and form a caseous mass, surrounded by more or less general tuberculous infiltration. Finally, the tonsil may be reduced to a stump formed by a mass of tuberculous tissue, the infiltration extending to the neighbouring connective tissue and muscle.

Some recent observations show that the tonsils are really very frequently tuberculous in cases of fatal tuberculosis, although in the majority of cases there is no naked eye evidence of tubercle. Hugh Walsham made a careful microscopic examination of the tonsils after death in twenty-four cases of chronic pulmonary tuberculosis, in seventeen of which he found tubercles; and in seven cases of acute pulmonary tuberculosis, in four of which he found tubercles. In these cases tubercles were generally in the miliary form, and only occasionally was there evidence of commencing caseation. They varied greatly in number in different cases. Bacilli were usually present, but scanty. Walsham's examinations of enlarged tonsils and adenoid growths removed during life proved negative.

The posterior wall of the pharynx is sometimes infiltrated and ulcerated. When this occurs, it is generally in connection with laryngeal tubercle.

Diagnosis.—The difficulties, as in the case of the tongue, occur in connection with syphilis and malignant disease. A careful examination of the lungs and of the sputum will probably reveal evidence of pulmonary tuberculosis, if the lesion is tuberculous. In doubtful cases, scrapings should be examined for bacilli, which are generally to be found in tuberculous cases.

Prognosis and treatment. — The prognosis is always grave. The presence of the disease interferes with mastication and deglutition, and usually is in itself evidence of extensive constitutional affection. The malady tends to recur if the ulcer is scraped and locally treated. In all advanced cases, the treatment can only be palliative. If there is pain, spraying or painting with cocaine before food will make mastication, etc., more tolerable. If the case is seen sufficiently early, and the disease is limited, an attempt may be made to remove the diseased tissue by scraping.

Unfortunately, it is very apt to recur, on account of the great difficulty in effecting a thorough removal. As in the case of the tongue, chlorate of potash and borax washes may be employed, and the ulcers may be dusted with the iodoform, morphine, and borax powder. Lactic acid may also be applied in the mode described under the heading of Tuberculous Disease of Larynx.

ŒSOPHAGUS, STOMACH, AND DUODENUM

Tubercle of the œsophagus is not common. According to Cone, up to 1897 only forty-eight cases had been recorded. Out of 531 cases of pulmonary tuberculosis at Brompton, tubercle of the œsophagus was found twice; in one case in the form of discrete tubercles, in the other of tuberculous ulceration. The œsophagus may be affected by extension from disease of pharynx, bronchial glands, or other neighbouring structures, by infection of pre-existing lesion, such as simple or malignant ulcer, by blood infection, or by inoculation of previously healthy mucosa by tuberculous sputum. Occasionally ulceration of the œsophagus, which is non-tuberculous, is met with in phthisical cases.

Tuberculous ulceration of the stomach is not so uncommon as that of the œsophagus. The ulcers are almost invariably secondary. They may arise by extension from the peritoneum, or through a general blood infection, or from ingested tuberculous material. The only primary case I know of is one recorded by Orlandi, in which there was primary tuberculous ulceration of the pylorus, extending to the serous coat and producing some narrowing of the orifice. Proof of the nature of the disease was established by inoculation, as well as by microscopic examination. There was another area of tuberculous infiltration in the small intestine, but no evidence of disease elsewhere. Ulcers have not very infrequently been met with in the stomach in cases of tuberculosis, but usually there has been no evidence of tuberculous deposit in their floor or in the vicinity. The probability is that most of these are simple ulcers. Marfan, in 1887, concluded that only twelve of the then recorded cases of tubercle of stomach were genuine. Forty-two cases of tuberculous ulcers of the stomach in 1180 autopsies on tuberculous children have been recorded in literature. Sometimes tuberculous ulcers of the stomach are multiple, as in cases reported by Alice Hamilton and W. D. Lister. According to Marfan, six cases of perforation of the stomach from tubercle have been observed, but always from without inwards. Perforation occurred in three cases from a tuberculous gland, while twice it was the result of peritoneal tuberculosis, and once was consecutive to a tuberculous ulcer in the transverse colon.

Tuberculous ulceration of the duodenum is less uncommon in adults than that of the stomach. Nine cases were met with among 531 autopsies on cases of phthisis at Brompton.

INTESTINE.

Etiology.—Intestinal tuberculosis is very common in connection with pulmonary tuberculosis, but rare apart from it. In 1000 autopsies upon tuberculous subjects at the Pathological Institute of Munich, in 567 there was intestinal tuberculosis, but only one of these was primary. Out of 1008 autopsies in cases of phthisis at the Brompton Hospital, intestinal tuberculosis was met with in 707 cases, or in 70·1 per cent. of the whole. The proportion of cases is sensibly the same for the two sexes, unlike

laryngeal tuberculosis. Thus 69·3 was the percentage for the males, and 72·1 that for the females.

There is little doubt that in all, or nearly all, the cases of phthisis the affection of the intestines is caused by the swallowing of the sputum. We have seen how readily animals are rendered tuberculous when fed with tuberculous material, and how, in such cases, the lesions, as a rule, are more marked in the intestines and mesenteric glands than elsewhere. Tuberculous milk may of course be the starting-point of infection of the intestines, but this cause will account for a very small proportion of the cases.

Soltau Fenwick and Dodwell, in a paper founded on 2000 necropsies at the Brompton Hospital, give the following particulars regarding the cases with intestinal tuberculosis:—

Duodenum affected	.	.	.	.	in 3·4 per cent.
Jejunum	.	.	.	.	„ 28 „
Ileo-cæcal region	.	.	.	.	„ 85 „
Ascending colon	.	.	.	.	„ 51·4 „
Transverse colon	.	.	.	.	„ 30·6 „
Sigmoid flexure	.	.	.	.	„ 13·5 „
Rectum	.	.	.	.	„ 14 „

From this table it will be seen that in 85 per cent. of the intestinal cases the ileo-cæcal region is affected, and from this part the frequency of the disease diminishes in both directions. The cæcum is the part most commonly affected. The vermiform appendix is affected in 58 per cent. In about two-thirds of the intestinal cases examined at Brompton, both the large and small intestine were affected; in about a fifth, the large intestine alone; and in about an eighth, the small intestine alone.

Morbid anatomy.—The forms in which tubercle is usually seen in the intestine are the grey miliary tubercle, or the larger yellow caseating tubercle, and ulcers of various sizes and forms. The tubercles are generally seated in the solitary follicles and Peyer's patches. The miliary tubercles are seldom seen alone, but occasionally the only lesion is the presence of a few caseous nodules here and there. The tubercles are seated in the mucosa or in the glandular structure itself. When they soften, the epithelium becomes undermined and necrotic, and the caseous contents are expelled, a small cup-shaped ulcer being formed with slightly overhanging edges. This gradually extends in depth and laterally. In Peyer's patches the process generally begins in separate spots, several small ulcers being formed, which gradually coalesce. The larger ulcers have somewhat everted, thickened edges. The process in such ulcers is a slower and more gradual one than in those with undermined edges. The floors of the ulcers may be smooth and clean, or irregular and caseous, being as a rule formed by the infiltrated muscular layer, but even that may be destroyed. Tubercles may often be seen in the floors and on the peritoneal aspect beneath the serous membrane. The ulcers, once formed, tend to spread: those in the solitary follicles, by extension, coalesce with one another, and with those in the Peyer's patches. The ulcers thus not uncommonly, instead of being longitudinal, become transverse to the course of the intestine.

As Treves has remarked, "the very nature of the tuberculous process and the usual progress of the trouble are strongly opposed to the formation of cicatricial tissue." Yet it sometimes happens that strictures result from tuberculous ulcers. A few cases have been recorded by Treves and others. Ulcers in the jejunum are, as a rule, few and far between, and generally confined to its lower part. The amount of disease present in the ileum

may vary from one or two small ulcers or tubercles to a very wide destruction of the mucous membrane. The process is almost invariably most extensive in the neighbourhood of the ileo-cæcal valve. The cæcum, it has been pointed out, is more commonly affected than any other part of the intestine, and sometimes is the only part which is diseased. When the cæcum is affected, it is very usual for the vermiform appendix to suffer also. As in the small intestine, so in the large, the morbid changes may vary from a few small tubercles to a very general ulceration. Both the extent and frequency of disease diminish as the rectum is approached. In the rectum the ulcers are usually of small size. Hæmorrhage from the floor of a tuberculous ulcer is decidedly rare. Intestinal perforation occurs in a little over 1 per cent. of all fatal cases of pulmonary tuberculosis. Thus it was met with twenty-five times in 2000 necropsies at Brompton. Of these, fifteen terminated in acute peritonitis, and ten in local abscess. In one of my cases, a perforative ulceration of the appendix led to a perityphlitic abscess.

Of recent years, a chronic hyperplastic form of intestinal tuberculosis has been recognised. It is characterised by great thickening of a limited portion of the bowel wall and narrowing of its lumen. It has been met with in the ileum, but most frequently occurs in the cæcum, giving rise to a carcinomatous-like tumour.

Fistula in ano is not a very common complication of tuberculosis, and yet a large proportion of the sufferers from fistula are tuberculous. The most complete statistics on the subject are those of Spillmann, who found among 14,730 cases of phthisis, 523 of fistula, or about 3·5 per cent. Among 1680 of my out-patients with pulmonary tuberculosis, I only met with twenty cases of fistula, giving a proportion of about 2 per cent. among males. Among 626 phthisical patients, Hartmann found and operated on thirty-one cases of fistula, the proportion being 6 per cent. in men and 3·5 per cent. in women. Of forty-eight cases of fistula, twenty-three were tuberculous, and in two more there was a tuberculous family history. Allingham gives a much smaller proportion. Phthisical symptoms existed in 234 out of 1632 cases of fistula, or in little over 14 per cent. Why tuberculous fistula should affect men in so much larger proportion than women, is not explained. The incidence we have seen of tubercle in the intestine is about equal in the two sexes. Ordinary fistula, moreover, is as common in women as in men. It is probable that in tuberculous cases the fistula begins with a tuberculous ulcer in the rectum, not very far from the anus, and in connection with this, an abscess forms which burrows until it finds its way externally.

Symptoms.—Miliary intestinal tubercle will produce no characteristic symptoms. The chief symptom of tuberculous ulceration of the intestines is persistent diarrhœa, the occurrence of which in a tuberculous subject is always suggestive. However, in some cases of ulceration, diarrhœa never troubles the patient, who may instead suffer from constipation. On the other hand, tuberculous patients may have persistent diarrhœa without ulceration. Pain and tenderness in the abdomen are sometimes experienced, but cannot be said to be characteristic.

It is very seldom that intestinal tuberculosis is primary, and accordingly it is difficult to distinguish the symptoms of the secondary from those of the primary disease. It is probable that pyrexia, sweating, wasting, etc., will be among the symptoms met with. Frequently, too, the symptoms of peritoneal tubercle will be added to those of intestinal.

Diagnosis and prognosis.—If one can ensure that the patient does not swallow any sputum, the discovery of tubercle bacilli in the stools will establish the nature of the case. There is a very strong probability in all cases of chronic diarrhœa in tuberculous subjects, that the cause is tuberculous ulceration. The prognosis is very unfavourable when ulceration has occurred. The possibility, but unlikelihood, of cure is shown by the rare occurrence of healed cicatricial ulcers.

Treatment.—It is very important in all cases of pulmonary tuberculosis to ensure that the patient does not swallow his expectoration. It is still important, in order to prevent further infection, that this should be impressed on him when ulceration of the intestines has already occurred. Little can be done in the way of checking or influencing the disease when once symptoms have become marked. It should be borne in mind that diarrhœa is not simply due to the presence of ulceration, but to the coexistence with the ulceration of a catarrhal condition of the intestine.

When the diarrhœa is acute and accompanied with pain and tenderness, the patient must be kept entirely at rest. The local application of warm poultices or fomentations will probably comfort and relieve. The diet may consist of cold boiled milk with lime-water, Benger's food, Savory and Moore's food, or other prepared malted food, and whites of eggs, either lightly boiled or diluted with water and flavoured with orange flower. Raw meat will sometimes be borne well. Isinglass, well-boiled rice, and arrow-root will usefully supplement the other foods. If stimulants are indicated, old brandy or port wine should be chosen. Sherries and champagnes should be avoided. Opium is a most valuable drug, and may be given alone in a liquid or solid form, or in combination with other drugs. Bismuth stands only second to opium. Of this, the most generally useful preparation is the subnitrate in doses of 10 to 20 grs. made up with mucilage and water, to which may be added 5 or 10 minims of tincture of opium or liquor opii sedativus, and a drachm of tincture of catechu. The salicylate of bismuth is preferred by some, as combining antiseptic properties with the special local action of bismuth. Its dose is the same as that of the subnitrate. Sometimes at the outset it is well to administer an aperient, in order to rid the intestine of any irritating substances. For this purpose a grain of calomel, followed by a small dose of castor-oil, is valuable. If the symptoms abate, the dietary can be gradually improved, and the opium and bismuth diminished or withdrawn.

In chronic cases, a too rigid dietary need not be enforced, but the patient should be forbidden fruit, green vegetables, and all articles of food likely to fret and irritate the intestines or to increase any tendency to diarrhœa. Tea, coffee, and beef-tea are generally better dispensed with. The preparations of bismuth and opium, already mentioned, are likewise valuable in chronic cases. The subgallate of bismuth (dermatol) is a useful astringent, and may possibly succeed in doses of 8 to 20 grs. when other preparations fail. A remedy which sometimes relieves the diarrhœa is sulphate of copper. A quarter of a grain of sulphate of copper, with half a grain of opium, may be given once or twice a day. Kino, in the form of the pulv. kino co., may also be tried in doses of 5 grs. Cotoin in 2 gr. doses in pill form or suspended in water and mucilage has occasionally proved useful. Sometimes the combination of lead and opium, as in the pil. plumb. c. opio, will relieve.

Tannigen and tannalbin, both derivatives of tannin, are astringents which have lately been used in these cases. They are given in doses of

10 to 20 grs. three times a day. Dilute sulphuric acid, in doses of 15 to 20 minims, may also be tried. No rules can be laid down as to which of these remedies will suit in individual cases. I have mentioned them in the order in which I have myself found them useful. Sometimes they all fail, sometimes one will succeed where the others have not benefited.

In all forms of diarrhœa, but especially where it depends on, or is associated with, ulceration of the rectum, morphine suppositories, or starch and opium enemata, may give more relief than anything else. As recommended by Walshe, enemata of nitrate of silver, 1 to 3 grs. dissolved in 4 oz. of water, may also have a beneficial influence.

Inguinal colotomy has been recommended in severe tuberculous ulceration of the rectum. In anal fistula there should be thorough opening up and treating from below.

LIVER AND PANCREAS.

The liver is generally the seat of miliary tubercles in acute general miliary tuberculosis. These bodies are, however, as a rule, not visible to the naked eye, although sometimes a few of the larger ones may be seen on the surface or in a section as greyish white masses as large as a pin's head. The formation of caseous tuberculous masses in the liver is so rare as to be a pathological curiosity. Occasionally the liver becomes honeycombed with innumerable cavities, varying in size from a pea to a walnut, and filled with softened bile-stained materials, while the walls contain tubercles. This form of disease is attributed to tuberculous affection of the bile-ducts.

A few cases have been recorded in which tuberculous abscesses have formed in the liver, varying from the size of a chestnut to that of a large orange. In a case which I have recorded, there was an abscess the size of an orange, containing soft pultaceous matter, surrounded by smaller caseous masses. There was thickening of the capsule of the liver, with contraction. There were tubercles with giant cells in the walls, and tuberculous disease of lungs. Similar cases have been recorded by Wethered and Mayo Robson. Some of the cases formerly recorded as scrofulous abscess of liver are now recognised as cases of actinomycosis. The pancreas, like the liver, is very rarely the seat of caseous or chronic tuberculosis. One case has been recorded by Ormerod where there were two or three small caseous patches, as well as a cavity which contained broken-down caseous substance.

TUBERCULOSIS OF THE LYMPHATIC SYSTEM.

LYMPHATIC GLANDS.

The identity of scrofula, or the enlarged caseating and suppurating glands met with in the neck and elsewhere, with tubercle, although maintained by Laennec and Villemin, was only firmly established when it was shown by Koch that the condition depended on the tubercle bacilli. Arloing has attempted to show that in scrofula the virus exists in an attenuated form, arguing from the fact that scrofulous matter does not infect rabbits, although it does guinea-pigs. It has been conclusively shown that there is no real difference in the virus, except that of quantity, the caseous matter from the scrofulous cervical or other glands being poor in bacilli, while that from the ordinary pulmonary lesions, etc., is rich. As already stated, for

an inoculation experiment to be successful, there is a minimum number of bacilli requisite, and no change is produced with a less number.

Etiology and morbid anatomy.—The lymphatic glands, particularly in the young, have a special liability to infection by tubercle. In 897 cases of tuberculosis in children, which I have collected, the lymphatic glands were affected in 792, or in 88 per cent., rather more than seven-eighths of the whole. It was maintained by Parrot that, in the case of the bronchial glands, the disease was always secondary to a pulmonary lesion, and further, that the condition in the lung was practically reproduced in the gland. It is certain, however, that at any rate in the case of children, the bronchial glands may be tuberculous without any tubercle being present in the lungs. It is common to find caseous bronchial glands in cases of tuberculous meningitis and general miliary tubercle. It seems clear, too, that disease in the lungs may be consecutive to disease in the bronchial glands. The observations of Loomis and Pizzini, who found that apparently normal bronchial glands of people dying from diseases other than tuberculosis produced tubercle by inoculation, require confirmation.

The lymphatic glands may become primarily infected in various ways —the cervical from the bacilli entering by the mouth and reaching the glands through the tonsils or some spot in the interior of the buccal cavity of little resistance; the bronchial through inhalation and the entrance of the bacilli by means of the lung; the mesenteric through ingestion, the bacilli being swallowed in the sputa or in milk or some other form of food, and passing from the intestine to the glands. In all these cases the glands may become affected without there being any actual tuberculous lesion at the spot where the bacilli have entered. Probably infection is often carried to the glands by the blood, and, as Watson Cheyne suggests, infection may follow on a non-specific inflammation.

Of the various glands, the most common to be affected in children, as well as in adults, are the bronchial. Moreover, as often happens when the bronchial glands are affected along with the mesenteric, the disease in the former is usually more extensive and further advanced. This points, as we have before remarked, to inhalation as probably the common mode of infection in children, as well as in adults. Whether the affected glands are bronchial, mesenteric, cervical, or other, the morbid condition is the same, and may conveniently be described here. The glands are swollen, soft, and of a greyish pink colour in the early stage, while later they may be firm and pigmented. On section, grey or yellow tubercles or spots of softening may be visible, but sometimes the tubercles are of too minute size to be recognised, except with the aid of the microscope. Sometimes the general swelling of the gland is simply inflammatory, but more commonly it consists of a tuberculous infiltration. Partial or general caseation of the tuberculous gland is the rule, but the fibrous change may supervene without caseation having occurred, and the gland becomes indurated and much pigmented, and contracts. Caseation may appear simultaneously at a number of separate foci, and spread until a large area or the whole of the gland is caseous. The caseous matter may soften, and the whole gland may have a pus-like consistency. The gland becomes adherent to the surrounding tissue, and the matter may burrow in various directions. Provided no other change supervenes, the caseous gland may become calcareous. This change is common in the case of the bronchial and mesenteric glands.

Symptoms.—The affection of the glands may be general or local.

General tuberculous adenitis.—It occasionally happens that there is a general affection of the glands throughout the body, a general tuberculous adenitis. This form of disease, to which special attention has been drawn by Fagge and Osler, is usually met with in adults, and runs a rapid and progressive course. It is decidedly uncommon, and no typical case of it has been met with to my knowledge at St. Thomas's Hospital during the last sixteen years. Osler states that it is more common in the negro than in the white.

The glands most likely to be affected are the axillary, cervical, bronchial, mesenteric, retroperitoneal, and inguinal. These may be much enlarged and caseous, while the various organs show little or no tubercle. The spleen, however, is usually enlarged, and may contain yellow caseous masses. Fever, which may be high, is generally present, and the patient rapidly emaciates. The duration of the malady is from six months to a year. Clinically, there is great difficulty in distinguishing it from lymphadenoma.

Local tuberculous adenitis. — *Cervical.* — The cervical glands very frequently become affected with tubercle in children, and sometimes also in adults. It was this form of the disease which was formerly described as scrofula. It is very common among the ill-fed and badly-housed poor, and large numbers of such cases come under treatment year by year at the hospitals. The disease in children is more often purely local, and unaccompanied by tuberculous lesions in the internal organs than otherwise; but in adults it is, in my experience, frequently associated with signs of disease in the lungs. Marfan believes that the so-called scrofula has a protective influence against pulmonary tuberculosis; but my own experience, like that of many others who see much of the latter disease, does not support this view. It is true that many who have had tuberculous glands in childhood never become phthisical; but, judging from the frequency with which one finds evidence of old scrofula among the phthisical, one cannot accept the protective theory.

The glands first enlarged are generally the submaxillary. These gradually increase in size, and are at first isolated, but later form nodular tumours. In about half the cases the enlarged glands suppurate, the skin becomes adherent, and an abscess opens spontaneously externally, unless incised. They are, as a rule, neither painful nor tender until there is suppuration and tension of the skin. They often progress very slowly. When they suppurate and communicate with the surface, they may go on discharging for a long time.

The treatment of such cases generally comes within the province of the surgeon. If there is an abscess, it should be opened. When the enlargement is considerable, and suppuration is suspected, it is generally best to remove the glands as thoroughly as possible; but, on account of their position and relations, it is not always practicable to remove the whole disease. Cod-liver oil, arsenic, good food, and bracing seaside air, such as that of Margate, have sometimes a favourable influence on the course of the disease, and the enlargement, after lasting some months, subsides, and the patient gets well. The fewness of the bacilli in these cases is probably the reason why general infection is decidedly uncommon. If the expectant method of treatment is adopted, the patient should be closely watched.

Bronchial.—The bronchial glands probably come next to the lungs as regards the frequency with which they become tuberculous. They are affected in about 80 per cent. of all cases of general tuberculosis, and in

about 40 per cent. of chronic cases. The glands most frequently affected are those situated just below the bifurcation of the trachea. When a tuberculous gland is embedded in the lung, it may be difficult to distinguish it from a diseased portion of lung.

Various symptoms have been attributed to tuberculous bronchial glands, especially crowing breathing, a paroxysmal cough, and vomiting, supposed to be due to irritation of the pneumogastric. Asthmatic attacks have been observed from pressure on the trachea or bronchus. Collapse of lung has also ensued. When the glands are large, any of the symptoms met with in mediastinal tumour may be present. Rarely a caseous gland perforates the trachea and causes fatal dyspnœa. The same accident has happened in the case of the œsophagus, the pericardium, the pulmonary artery, and even the aorta, which have all at times been perforated by caseous bronchial glands.

Mesenteric.—Similar changes to those just mentioned in the bronchial glands are frequent also in the mesenteric, and are often associated with tubercle of the intestines and peritoneum. The symptoms present are wasting and diarrhœa, with enlargement of the abdomen, in which nodules may be felt. They are more fully discussed in the section on tuberculous peritonitis. Perforation of the intestine sometimes occurs through a caseous mesenteric gland ulcerating through from without inwards. Just as obsolete tubercle is unexpectedly met with in the bronchial glands, so it is in the mesenteric. Sometimes one finds calcareous masses as large as a pigeon's egg, and smaller masses are not uncommon.

SPLEEN.

The spleen is very commonly affected in general miliary tuberculosis, especially in young children. It becomes moderately enlarged. Grey miliary tubercles are most easily recognised on the surface. Caseous tubercles may be more or less numerous, varying in size from a millet seed to a hazel nut.

LYMPHATICS.

As it is by means of the lymphatics that the bacillus reaches the glands, it is to be expected that the former should themselves sometimes be affected with tuberculosis. It was pointed out long ago that in the case of tuberculous ulcers of the intestine there are often to be seen on the serous surface little granulations, from whence proceed rows of similar bodies, arranged like the beads of a necklace. These follow the course of the lymphatics, of which they occupy the wall, and end in caseous glands. Similar granulations have been observed in the lymphatics of the pleura in connection with lesions in the lung.

It is in the subcutaneous lymphatics that the most interesting tuberculous lesions have been met with. These are nearly always secondary to such cutaneous inoculations as anatomical tubercle, warty tuberculosis, etc. Three cases are recorded where the primary cause was cutaneous tubercle of the finger, contracted by women while nursing phthisical husbands. They occasionally but rarely result from deep tuberculous lesions of the bones.

At intervals along the superficial lymphatics there are tumours, at first small, but gradually increasing to the size of a walnut or even a Tangerine orange. At first the skin is movable over them, and they are hard. As

they increase in size they soften and raise, redden and thin the skin, through which they gradually ulcerate, and discharge thin grumous pus, which contains few bacilli. There may or may not be a hard cord uniting the abscesses. The glands may be tuberculous also.

Eve has recorded a very typical case, in which there were three superficial fluctuating swellings in linear series along the forearm, in addition to one on the dorsum of the hand. The abscesses tend to recur, and in several of the recorded cases the patients ultimately died of phthisis.

TUBERCULOSIS OF THE VASCULAR SYSTEM.

Tubercle of the heart is uncommon. Miliary tubercle is sometimes seen on the surface, and rarely on the interior in cases of generalised tubercle. The conus arteriosus is a seat of election. Caseous masses are very rare. Cases of tuberculous endocarditis have been recorded by Lancereaux and Benda.

Tuberculous phlebitis and endarteritis have been frequently observed in acute miliary tuberculosis. Weigert found the condition in thirteen out of fourteen cases of this disease, commonly in the pulmonary veins. Mugge, in nine cases out of ten, found tuberculous granulations in the internal tunic of the pulmonary artery, as well as in the pulmonary veins. Hanau found the same condition in eight out of thirteen cases. Turner recorded a case in which there were clusters of minute granulations on four divisions of the pulmonary artery.

Cornil has observed a thickening of the intima with the new formation of a great number of cells of varied form, and among them numerous and very large giant cells. In consequence of the thickening of the intima the vessels become gradually blocked. Tuberculous growths have been met with in the large blood vessels, but are decidedly rare. In a few cases the aorta has been involved by direct extension from a tuberculous lesion external to the vessel. In other cases, tuberculous nodules have been found growing from the intima and projecting into the lumen of the aorta. In the reported cases, these have been few and of small size, seldom larger than a pin's head.

TUBERCULOSIS OF THE SEROUS MEMBRANES.

PLEURA.

Tuberculous pleurisy has of late years been recognised to be a much commoner disease than was at one time supposed. Many of the cases formerly described as simple idiopathic pleurisy, are now known to be really tuberculous. Some authorities, especially those of the French school, go so far as to assert that pleurisy *a frigore* does not exist. Germain Sée, probably expresses the truth, when he says that tuberculosis is the most usual cause of the so-called simple pleurisy, and represents the real cause in three-fourths of the cases.

Etiology, pathology, and morbid anatomy.—The evidence as to the nature of simple idiopathic pleurisy rests on the results of post-mortem examinations ; the examination of the exudation for bacteria, and the results obtained by inoculating animals with the fluid ; the result of the employment of tuberculin in patients affected by simple pleurisy ; and the subsequent history of the patients who have had an attack of pleurisy.

The evidence of the post-mortem room. Simple idiopathic pleurisy very seldom proves fatal, and on this account the evidence forthcoming from the post-mortem room as to its nature is very limited. During twelve years, 531 cases were admitted to St. Thomas's Hospital for pleurisy. Of these only fourteen died, of which three were complicated with pneumonia, one with pericarditis, and one was secondary to cardiac disease. Of the remaining nine, four were certainly tuberculous. Kelsch and Vaillard found tubercle present in the pleura in sixteen cases of what clinically appeared to be simple idiopathic pleurisy, in most of which the lungs were free from tubercle. Osler carefully analysed the post-mortem records of 101 cases from his wards, in which pleurisy—fibrinous, sero-fibrinous, hæmorrhagic, or purulent—was found, and of these there were thirty-two in which the pleurisy was definitely tuberculous. In Osler's cases, however, the pleurisies were for the most part secondary to acute diseases of the lungs, or occurred as terminal processes in chronic affections of the heart, arteries, or kidneys.

The serous effusion from a case of idiopathic pleurisy is nearly always found to be sterile, and apparently free from micro-organisms. The results of the inoculation of animals with the fluid show, however, conclusively that the tubercle bacillus, or its spores, if such exist, must in many cases be present in the fluid. The same difficulty has been experienced in discovering bacilli in milk where inoculation experiments have pointed to their presence.

Inoculation does not always succeed in producing tuberculosis, even when the pleurisy is undoubtedly tuberculous. Kelsch and Vaillard, as well as Gilbert and Lion, have recorded failure in cases subsequently proved to be tuberculous at the post-mortem examination. Netter found that out of sixteen cases certainly tuberculous, only eight gave positive results. In twenty-five cases of what were considered to be ordinary pleurisy, he succeeded ten times in inducing tuberculosis. He does not mention the amount used for injection, which, when dealing with a fluid in which tubercle bacilli are extremely few, is a matter of great importance.

Chauffard and Gombault injected into the peritoneal cavities of guinea-pigs 3 c.c. of serum from cases of pleurisy, and found that the fluid, in ten out of twenty cases, produced tuberculosis. Aschoff has recently obtained still more striking results. He also injected 3 c.c. of the serum into the peritoneal cavity. Out of twenty-five cases where the pleurisy was either certainly or probably tuberculous, eight gave a negative result, or 32 per cent. Out of twelve idiopathic cases, only three gave a negative result, or 25 per cent. The experiments of Eichhorst go to show that the larger the amount of serum used for injection, the smaller is the proportion giving negative results. When 1 c.c. of fluid was injected into the peritoneal cavity of guinea-pigs, in ten out of eleven cases the animals remained healthy, in the other a tuberculous affection of the lymphatic glands was caused. As in some of the negative cases tuberculosis was suspected, in later experiments larger quantities, as much as 15 c.c., were used for injection. When this was done, fifteen out of twenty-three guinea-pigs were infected, or 65 per cent. In other words, two-thirds of the cases of serous pleurisy proved to be tuberculous.

The amount of evidence as to the tuberculous nature of pleurisy through the use of tuberculin is small. The official report of the Prussian Government on tuberculin contains the accounts of fifteen cases of pleurisy

injected with it. Thirteen of these reacted. This, of course, does not justify the conclusion that the pleurisy itself was tuberculous, but it shows the probable presence of tubercle in a very striking proportion of the cases of pleurisy tested. Osler mentions an instance where a marked reaction from tuberculin led to a wrong diagnosis, the case eventually turning out to be one of cancerous pleurisy.

It has been observed by various physicians that a considerable proportion of patients who have suffered from pleurisy, later on are attacked by tuberculous disease of lung. Fagge remarked how one is frequently seeing patients who, having favourably passed through an attack of pleurisy, are shortly afterwards seized with hæmoptysis, or show signs of tuberculous disease of the lungs. Barrs of Leeds, in 1890, traced the subsequent history of fifty-seven patients treated for pleurisy in the Leeds Infirmary between 1880 and 1884. He found that thirty-two were dead, and eighteen of these were ascertained to have died from tuberculosis. Ziemssen says that of adults who have lived through a chronic pleurisy nearly one-half die of tubercle. Statistics similar to those of Barrs have been brought forward by Fiedler, Ricochon, and Bowditch.

Fiedler's statistics are founded on 112 cases which were aspirated by him at Dresden. Of these, twenty-five died of tuberculosis, sixty-six became certainly or probably tuberculous, and only twenty-one were in good health one or two years after. Bowditch's statistics are of great interest, because they were drawn from cases in private practice, and embrace an experience extending over many years. Out of forty-nine cases of pleurisy seen between 1849 and 1869, twenty-two died from phthisis; and of forty-one seen between 1869 and 1879 there were ten deaths from phthisis. As the investigation was made in 1889, sufficient time had probably not elapsed in the cases in the last decade to allow for the evolution of the proper quota of cases of phthisis. These statistics bring out prominently enough the frequency with which phthisis follows an apparently simple pleurisy, and strongly support the view that the pleurisy was itself tuberculous.

That empyemata are sometimes tuberculous is well known, but they are less commonly so than simple serous pleurisies. According to Netter, 25 per cent. of empyemata in the adult are tuberculous, and 6·5 per cent. in the child.

Tubercle bacilli are less difficult to stain and discover in purulent effusions than in serous—a fact which has been explained by supposing that in the former the bacilli are set free from the tuberculous ulcers of the pleura, while in the latter they are retained in the fibrin, which coagulates on the walls. Still their discovery involves great technical skill and patience. Ehrlich has found bacilli in each one of a series of cases examined by him, but often only as the result of examining an immense number of preparations. The absence of streptococci, staphylococci, and pneumococci in the pus makes it very probable that the case is tuberculous even if the tubercle bacillus is not found. A more certain mode of determining whether the pus is tuberculous or not is by inoculation in guinea-pigs. Out of thirteen cases of tuberculous empyema observed by Netter, in twelve, inoculations in guinea-pigs rendered them tuberculous, and out of six cases Straus succeeded in all.

It is doubtful whether there is a family history of tubercle in as large a proportion of cases of tuberculous pleurisy as in cases of pulmonary tuberculosis. Sittmann noted a family history in 24 per cent., which is a

lower proportion than for phthisis. Every one who sees a large number of cases of pulmonary phthisis must have been struck by the relative frequency of pleurisy as an antecedent in these cases.

Osler (Shattuck Lecture) has given a very useful classification of the varieties of tuberculous pleurisy.

1. Acute tuberculous pleurisy—(*a*) Primary, (*b*) secondary and terminal, (*c*) acute tuberculous suppurative pleurisy.

2. Subacute and chronic—(*a*) With serofibrinous effusion, (*b*) with purulent exudation, (*c*) chronic adhesive tuberculous pleurisy.

In the ordinary acute form, whether primary or secondary, the condition appears to be one of acute miliary tuberculosis of the membrane with a serofibrinous or hæmorrhagic exudation. The amount of the effused serum may be very large or never more than a few ounces. There is nothing characteristic about its appearance. It has already been pointed out that it is usually sterile. A hæmorrhagic character suggests either tubercle or new growth. The acute cases with purulent effusion are decidedly rare. They run a rapid course. The pus has been observed to be located in small pockets instead of forming a regular empyema. The membrane is frequently lined with a layer of fibrinous lymph, which may be of considerable thickness. Such cases pass into the chronic form, in which the pleura becomes greatly thickened—the thickening, however, being more marked in the case of the parietal pleura than in that of the visceral layer. The parietal pleura may form a layer two-fifths of an inch thick, or even more in the case of the diaphragmatic layer. The visceral layer is only a third or half as thick. Its surface is sometimes smooth and greyish white in colour, and sometimes honeycombed with deep irregular ulcers. In section one sees either with the naked eye or under the microscope distinct tubercles. When the case has become chronic, the two thickened layers of the pleura may be generally quite adherent and form a membrane nearly an inch thick, made up of fibrous tissue with perhaps here and there layers of caseous material. On the other hand, adhesions may not be general, but fluid may be collected in pockets in various situations. Occasionally the fluid in one pocket may be serous, while in another it may be curdy or even purulent. The effusion in the chronic cases may be either serofibrinous or purulent. The serofibrinous effusion may be very large in amount, and frequently re-accumulates again and again after tapping. The fluid is not so frequently hæmorrhagic as in the acute cases. Tuberculous empyema is essentially very chronic. The effusion is never absorbed spontaneously, and very rarely makes its way into a bronchus or discharges internally. The fluid is often thinner than ordinary pus, and it may not be truly purulent, but its purulent appearance may be due to the presence of suspended fatty matter.

Symptoms.—The symptoms and physical signs of tuberculous pleurisy are those of ordinary pleurisy, pain in the side, shortness of breath, and fever, together with friction or the physical signs of effusion There is no means of distinguishing the one from the other, apart from evidence of tubercle elsewhere, or the proof of the tuberculous nature by means of inoculation or otherwise as already described. Tuberculous cases, however, are apt to become chronic, and thus fever becomes persistent or effusion recurs. In a case of this kind under my observation, the continuance of the symptoms suggested the existence of a loculated empyema which was explored for in vain. The true nature of the case was only revealed when cerebral symptoms declared themselves.

The patient died from meningeal tubercle. In the case of tuberculous empyema there are fewer symptoms and less disturbance of the general health than in ordinary empyema. The effusion may be extremely large. The same remarks apply to this form as to the ordinary serous form.

Diagnosis.—The diagnosis of tuberculous pleurisy often presents great difficulty; but it must be remembered that, in a case of acute idiopathic pleurisy, tubercle is the most likely cause. Where it is important to give a positive diagnosis, the inoculation of 3 to 15 c.c. of the serous effusion into the peritoneum of a guinea-pig may be tried. The discovery of evidence of tubercle elsewhere will be valuable. After recovery from an attack of pleurisy, it may be worth while to test the patient with tuberculin. In cases with purulent effusion the tubercle bacillus may possibly be discovered. Probably the most frequent mistakes are made between ordinary empyema, especially when the fluid is encysted, and tuberculous pleurisy. The only way to avoid missing an empyema is to use the exploring needle or aspirator whenever there is a suspicion of pus.

Prognosis.—The prognosis of primary tuberculous pleurisy is as regards the immediate attack decidedly good. This is shown by the small number of deaths. A large number, however, as is shown by the statistics already brought forward, develop tubercle elsewhere sooner or later. Where the pleurisy occurs as a secondary condition, it adds to the gravity of the already existing disease; but, as a rule, the immediate prognosis is not unfavourable. Some authorities are of opinion that the presence of an effusion in the pleura has a beneficial influence on a lung affected by tubercle. The prognosis in tuberculous empyemata is naturally not so favourable as that of non-tuberculous. The former often become chronic, and terminate fatally.

Treatment.—The treatment of tuberculous pleurisy embraces all those measures which have been found to be useful in the ordinary disease. In the early stages where there is pain, rest and fixation of the side by belladonna strapping give relief. Aspiration may have to be frequently repeated when the disease becomes chronic. Counter-irritation by means of iodine or by blistering is sometimes useful in promoting the absorption of the fluid. Graduated exercises may help to bring about the re-expansion of the lung. After recovery from an attack of pleurisy, it is of the highest importance that the general health should be re-established, and, where it is possible, the patient should spend one or even two winters abroad, or, if a good sailor, he might take a long sea voyage with advantage.

PERICARDIUM.

Tuberculous pericarditis is decidedly rarer than similar affections of the pleura and peritoneum.

Etiology.—It is much more frequently secondary than primary. It is usually associated with, and secondary to, tuberculosis of the bronchial and anterior mediastinal glands. In a considerable proportion of cases, tubercle of the peritoneum, pleura, or lungs is also present. It may occur at any age, and cases have been noted in infants under a year, as well as in old people. Virchow recorded a primary case in a man of 81, in whom, moreover, this was the only lesion. It appears to be more frequent in males than in females. The following particulars may help to indicate the relative frequency of its occurrence.

Dietrich and Frerichs found tubercle of the pericardium in nine out of

578 cases of tuberculosis. Osler, out of 275 cases with tuberculous lesions at the Montreal Hospital, noted seven in which the pericardium was involved. Wilson Fox found it once in ninety-three cases of phthisis. Out of 645 cases of pulmonary tuberculosis at the Brompton Hospital, there were fourteen in which adherent pericardium was found, and there were fourteen in which there was recent pericarditis. In about half of the latter cases, which were examined microscopically, tubercle was found. Lebert states that tubercle exists in 20 to 25 per cent. of all cases of pericarditis, while Bamberger makes the proportion 14 per cent.

Morbid anatomy.—It is not uncommon in general miliary tuberculosis to find miliary tubercles present on both layers of the pericardium, but as a rule they are not numerous. When pericarditis occurs, the development of grey miliary tubercles in the pericardial membrane is accompanied by an injection of the vessels in their neighbourhood, with which may be associated small hæmorrhages. Subsequently there is a deposit of fibrinous lymph on the surface of the membrane, embedding and obscuring the tubercles. This may be preceded or followed by an effusion into the pericardial sac, generally a somewhat turbid serum, in which are suspended flakes of lymph. The effusion may be blood-stained or purulent, but the latter is decidedly rare. The amount of effusion may be very large, and the pericardial sac greatly distended. Musser has recorded a case where at the post-mortem the sac contained 64 oz. of bloody serum, while 37 oz. of similar fluid were removed by aspiration during life. Most commonly the amount of fluid is small and becomes absorbed, while adhesions form between the two layers of the pericardium, the sac of which is gradually obliterated in whole or in part. The parietal layer in the recent stage is generally considerably thickened and œdematous. In a case of old standing, or even in a recent case where there is much deposit of fibrinous lymph, it may be very difficult or even impossible to recognise the presence of tubercles with the naked eye. It is only by cutting sections and examining microscopically, that the true nature of such cases can be determined. In old cases both layers of the pericardium are thickened, sometimes very much so.

Symptoms.—The symptoms and physical signs of tuberculous pericarditis do not differ essentially from those of the ordinary affection. In many cases the malady remains latent and is only discovered accidentally at the post-mortem. In other cases the usual acute symptoms of pericarditis are present. In the chronic adhesive cases, the symptoms, when such exist, are those of chronic congestion of the lungs, liver, etc. The physical signs are numerous, and, as a rule, not conclusive as to the nature of the affection.

Diagnosis.—The tuberculous nature of pericarditis is always probable when it occurs in a tuberculous subject in whom other causes, such as rheumatism and renal disease, are unlikely. Apart from the evidence of tubercle in other organs, and the absence of other causes of pericarditis, there is little to help us in arriving at a diagnosis. An unusually protracted course and an irregularly febrile temperature are in favour of tubercle. If paracentesis is performed, the presence of blood in the exudation favours tubercle. An examination of the exudation for bacilli or inoculation experiments in animals may sometimes afford conclusive evidence as to the nature of the case.

Prognosis and treatment.—The prognosis when a case of pericarditis can be diagnosed as tuberculous is certainly unfavourable. There is no reason why, when the tubercle is limited to the pericardium, recovery

should not frequently take place. These, however, are just the cases in which diagnosis fails. Tuberculous pericarditis calls for no special treatment other than would be adopted in the ordinary disease. Osler speaks highly of the continuous application of the ice-bag or Leiter's coils as allaying pain and checking the tendency to effusion.

PERITONEUM.

Etiology.—Tuberculous peritonitis is frequently associated with the presence of tubercle in other parts, especially in the pleura. Tuberculosis of pleura coexisted in seventy-five out of 167 cases of tuberculous peritonitis collected by Osler. The disease is frequently primary in the peritoneum, but how the virus reaches it is not clear. It is not uncommonly secondary to pulmonary tuberculosis. Thus it was found in fifteen out of 382 cases of pulmonary tuberculosis examined post-mortem at the Brompton Hospital. It is common in children, but may occur at any age of life. Statistics, however, are useless to illustrate the age distribution. Thus, out of 100 cases collected by Hawkins at St. Thomas's Hospital, forty-three occurred in children under 10; while out of 357 collected by Osler, only twenty-seven were in children under 10. It is a disputed point whether it is more common in males or females. Fagge found the disease more than twice as common in men as in women. Osler says it is certainly more common among females. The statistics of surgeons show the disease to be more common among females; those of the post-mortem room show it to be more common among males.

A considerable number of cases have been observed where tuberculous peritonitis coexisted with cirrhosis of the liver. As I have pointed out, alcoholic subjects appear to be more liable to tubercle than those who are temperate.

The association of tuberculous peritonitis with similar disease of the Fallopian tubes deserves to be specially mentioned. The latter are found to be affected in from 30 to 50 per cent. of the fatal cases in women. It is difficult in these cases to decide in which part the disease has originated. Although the fimbriated extremity of the tube is in many instances the most markedly diseased, this does not prove that infection has come *viâ* the peritoneum, for, as has been pointed out by Whitridge Williams, this portion is much more vascular than the rest, and therefore the most likely to be affected by blood infection.

Morbid anatomy.—It is not at all unusual, in association with tuberculous ulcers of the intestines, to see a deposit of grey translucent granulations on the peritoneal surface in the neighbourhood of the ulcers. Sometimes, on the peritoneal aspect of the ulcers, there is a local deposit of fibrinous lymph. It is seldom, however, that there is a general tuberculous infection of the peritoneum.

Sometimes, as a part of general miliary tuberculosis, there is a distribution of small miliary tubercles on the surface of the peritoneum, most abundant on the parietal layer. When tuberculous peritonitis occurs, grey miliary tubercles appear over a wide area of the serous membrane, but especially on the under surface of the diaphragm and on the parietal peritoneum in the flanks. These may attain the size of a hemp seed, and may be associated with larger yellow caseating nodules. In more severe cases the granulations appear in the deeper connective tissue in the mesentery and great omentum. In addition, a

number of caseous masses, due to the coalescence of smaller tubercles, may be met with. There is generally an effusion of fluid into the peritoneal cavity, sometimes large in amount. The fluid is at first clear yellow serum, but may contain fibrinous floccules.

When the tubercles are numerous, the membrane becomes covered with a layer of fibrinous lymph, and the coils of intestine are apt to become adherent to one another and to the abdominal wall. In some cases a general obliteration of the cavity may take place. The effused fluid often undergoes absorption in whole or in part at a later stage, or it may become puriform. As the result of adhesions, it is apt to become encysted, especially in the dependent parts. At a later period the pus may dry up.

The great omentum is frequently the seat of a deposit of caseous tubercle. It then becomes thickened, contracted, adherent to the intestine and abdominal wall, and may form, as already mentioned, a transverse bar-like tumour lying across the abdomen about the level of the umbilicus. The mesentery may also be the seat of similar changes, so that it becomes thickened and contracted, and the small intestines are massed together about the middle of the abdomen.

At the post-mortem it is often extremely difficult to obtain a correct idea of the true state of affairs. The intestines are bound together in all directions, and firmly glued to the abdominal wall, the great omentum, and the various organs. The only feasible method of examining the case is to cut sections in various directions. In making these sections, one comes on collections of pus or serum or caseous deposits. Sometimes it is found that the intestines have been perforated in various situations, and that, as a result, fæcal abscesses have formed.

Symptoms.—Tuberculous peritonitis sometimes manifests no decided symptoms, and symptoms when present may not only be vague but also misleading. When it occurs in the course of pulmonary tuberculosis, there may be little or nothing to attract attention to the abdominal condition. In many of the cases which have been treated by laparotomy, apart from the existence of a tumour or evidence of disease of the pelvic organs, there has been no indication of the nature of the disease. This variety may be spoken of as the *latent* form of the disease. Besides this there are two main forms—an acute and a chronic variety.

The acute form has been already described as the abdominal form of acute miliary tuberculosis.

In the chronic form, the symptoms, while similar to those met with in the acute form, are of less severity and of longer duration.

It must be clearly borne in mind that the acute may pass into the chronic form. The temperature is variable. There may be some pyrexia such as exists in the acute cases, but more commonly the temperature varies little from normal, or it may be persistently subnormal. Frequently the most marked feature of chronic cases is the presence of a tumour, which may lead to erroneous diagnosis of ovarian tumour or malignant disease.

The most common tumour is a transverse bar-like mass situated at or slightly above the level of the umbilicus, formed by the thickened, infiltrated, and rounded great omentum. This mass may be mistaken for the lower border of an enlarged liver, but can usually be distinguished from it by observing the presence of resonance above it.

In some cases there are sacculated collections of fluid lying in pockets formed by adherent coils of intestine, the abdominal wall, the

mesentery, and the pelvic or other organs. Such tumours may be altogether fluid, or they may contain caseous masses embedded among the parietal adhesions, giving them a nodular character. These tumours, due to encysted fluid, have been specially studied by Osler, who has subdivided them. First, those in the upper region of the abdomen, which are most commonly met with in connection with perihepatitis. Second, those in the middle region—those in which the entire anterior portion of the peritoneal cavity is occupied by a single collection of fluid; and those in which there is a more limited sacculated exudation on one or other side of the abdomen or in the middle line. Third, sacculated collections in the pelvic region, in the case of females, which are nearly always connected with disease of the Fallopian tubes. It is these tumours that are so frequently mistaken for ovarian disease, and many laparotomies have been performed under this impression.

Thickened and retracted intestinal coils sometimes form a tumour of great distinctness. Such a formation is most common in the cæcal region. Enlarged mesenteric glands give rise to a lumpy feeling of the abdomen. This is more common in children than in adults.

Although such tumours are a common feature of chronic tuberculous peritonitis, they are not always met with. When there is no tumour, the abdomen is generally large and doughy. Ascites usually exists at some period, but not to a marked degree. A considerable proportion of the chronic cases get well.

Diagnosis.—The acute form.—These cases are often at first mistaken for enteric fever, which is not excluded by absence of spots and of enlargement of spleen. Evidence of tuberculous disease elsewhere will make tuberculous peritonitis more probable. The character of the temperature, which wants the regularity of enteric fever, may help. It is sometimes only after the disease has lasted an unusual time for enteric fever, that its true nature is suspected. Serum diagnosis should be employed in all doubtful cases.

In the chronic form, the principal difficulty is in excluding ovarian tumour and malignant growth. As regards ovarian tumour, the most important points are the normal temperature and the absence of disturbances of the digestive organs, and of signs of disease in the tubes, lungs, or elsewhere. The tumour itself is usually not so well defined as an ovarian, but in exceptional cases no difference can be made out. When malignant disease exists, there is usually more emaciation, a greater degree of cachexia, and greater constitutional disturbance. Cases of chronic tuberculous peritonitis with a considerable amount of ascites are sometimes mistaken for ascites connected with cirrhosis of the liver. The difficulty is all the greater, inasmuch as the two are sometimes associated, and tuberculous peritonitis may be met with in intemperate subjects. In such cases the association of unilateral pleural effusion, the course of the temperature, etc., may help.

Prognosis.—It is now recognised that a considerable proportion of cases of tuberculous peritonitis recover. Of 100 cases treated at St. Thomas's Hospital, Hawkins records that forty proved fatal, while at least twenty-one made good recoveries, remaining well for from nine months to nine years. The prognosis is better between the ages of 5 and 10 than at any other period. In patients over 20 years of age quite a large proportion prove fatal. The presence of extensive disease of lung, a history of alcoholism, the coexistence of tuberculous disease of the pleura, pericardium, uterine

appendages, etc., are all unfavourable points. Cases where there are sacculated collections of pus are especially unfavourable. When the disease is discovered unexpectedly during a laparotomy, the prognosis is favourable.

Treatment.—The treatment of tuberculous peritonitis divides itself into hygienic, medicinal, and operative. The first two methods should always have a fair trial. The patient should be kept at rest, but as far as possible should lead an open-air life. Bracing sea air, such as that of Margate, Cromer, or North Berwick, is specially useful. Plain, wholesome, and nutritious food should be given, such as is adapted to the state of the bowels, being laxative when there is constipation, and *vice versâ*. The appetite and digestion may be improved by the administration of a simple alkaline tonic. Where there is diarrhœa, bismuth is very valuable. The subnitrate, the subgallate, or the salicylate, in doses of 5 to 20 grs., may be given with or without opium, the dose being adapted to the age of the patient. Cod-liver oil, when well borne, is very valuable, but care should be exercised not to spoil the appetite and digestion by too large a dose, or by giving it at all where it excites nausea. The remarks under the head of Treatment of Pulmonary Tuberculosis apply with special force here. Pancreatic emulsion and petroleum emulsion are also useful. The syrup of phosphate of iron or iodide of iron may prove beneficial in doses of 20 minims to 1 drm. French authorities speak highly of the *sirop iodotannique*, a combination of iodine and tannin.

Local applications to the abdomen have been found valuable. Thus Fagge speaks very highly of linimentum hydrargyri spread on flannel and kept continuously closely applied to the abdomen. Various liniments, such as the linimentum ammoniæ, or lin. tereb. acet., may be gently applied with rubbing. Probably the massage is of benefit independently of the application. Marfan recommends painting the abdomen with tincture of iodine, followed by a coating of flexible collodium, the application to be renewed weekly or once a fortnight. This, he says, immobilises the abdominal wall, keeps the organs at rest, and diminishes hyperæmia.

In cases where no improvement results, after four to six weeks in acute cases, and after four to six months in chronic cases, laparotomy may be resorted to. The increase or continuance of ascites and pyrexial temperature are the chief indications for this measure. A free incision should be made, and the fluid thoroughly evacuated. If the fluid is serous, the wound is at once closed. When the fluid is purulent, a drainage tube must be left in for a short time.

How laparotomy acts in these cases is not satisfactorily explained, but the results, on the whole, have been good. It came into vogue on account of the good results which followed the operation at the hands of Spencer, Wells, and König. The earliest cases were done for purposes of exploration, and tubercle being found, no improvement was expected. It proved quite otherwise, and the operation has since been frequently performed with equally successful results.

Nannoti and Baciochi induced tuberculous peritonitis in dogs and rabbits. A certain number were subjected to laparotomy, and the remainder left to themselves. The results in the case of the dogs were the more striking. Of those which underwent laparotomy, seven recovered and two were not benefited. Of those left to themselves, only one recovered. From the changes found in the animals which recovered, the authors infer " that the operative interference stimulates or increases the

reparative changes by the mechanical influence which it exerts on the impressionable peritoneum."

<h2 style="text-align:center">MULTIPLE SEROUS TUBERCLE.</h2>

Although we have given separate descriptions of tuberculous pleurisy, peritonitis, and pericarditis, it must be borne in mind that these affections are frequently combined. This, it has already been pointed out, is especially likely when the peritoneum is one of the membranes involved.

<h1 style="text-align:center">TUBERCULOSIS OF THE RESPIRATORY SYSTEM.</h1>

<h3 style="text-align:center">NOSE.</h3>

Tuberculosis of the nasal membrane is rare. Considering the frequency with which the tubercle bacillus is found in the nasal cavities, the rarity of the disease shows how great must be the resisting power of the mucous membrane. It is sometimes primary, but more commonly is secondary to pulmonary and laryngeal tuberculosis. It shows itself either under the form of ulceration or tumour or both. Tumour is usually met with in primary cases, ulceration in secondary. The seat of ulceration is preferably the septum cartilagineum, of tumour the turbinated bones. It occurs at any age, but most frequently between 10 and 40. It is equally prevalent in the two sexes. The ulcers are generally shallow and surrounded by elevated soft margins showing miliary tubercles. The tumours are rounded or elliptical, with a granular surface, greyish or greyish yellow, of soft consistence and easily made to bleed. The disease may by extension involve the naso-lachrymal duct and the conjunctiva.

Symptoms may be purely negative. Pain is rarely present. In the ulcerative variety, there may be profuse muco-purulent discharge, which is often fœtid and sometimes mixed with blood. On examination with the nasal speculum, the affected side of the nose is probably found to be filled with crusts, on removal of which the characteristic ulcers will be seen. Tumour will probably produce obstruction to the breathing.

Diagnosis, prognosis, and treatment.—Syphilis and new growth may be difficult to eliminate. In secondary cases, evidence of tuberculosis elsewhere will help. In primary cases, it may be impossible to decide the nature of the disease without microscopic examination of a portion of the growth or the discovery of the bacillus in the scrapings. The course of the disease is very chronic. It is apt to relapse when surgically dealt with. It is not in itself dangerous to life, but may be complicated with meningitis, etc. Constitutional remedies should always be employed. New growths should be removed as thoroughly as possible. Ulcers should be scraped and treated with lactic acid or cauterised, the same precautions being taken as in the case of laryngeal tuberculosis. Cleansing and disinfection of the nasal cavity is always important.

<h3 style="text-align:center">LARYNX.</h3>

Etiology and morbid anatomy. — Laryngeal tuberculosis is rarely primary. As commonly met with in practice, it is secondary to pulmonary phthisis, in the course of which it is usually a late phenomenon.

Its frequency is shown by the following statistics. It was met with in 472 cases out of 1008 autopsies at the Brompton Hospital. This gives the large proportion of 46·8 per cent. This is a considerably higher percentage than that given by Heinze, who met with 376 cases of laryngeal ulceration among 1226 cases of pulmonary phthisis, giving 30·6 per cent.; but Heinze thinks his estimate is too low, for in 184 cases where the larynx was specially examined, it was found to be affected in 38 per cent. Frerichs in 250 cases of chronic phthisis found the larynx affected in 101, or in 40·4 per cent. Ivall in 1000 post-mortems found the larynx affected in 239. Males are not only actually but relatively more frequently the subjects of laryngeal tuberculosis than females. Thus the males affected with laryngeal tuberculosis were three times as numerous as the females at the Brompton Hospital, while during the same period the males affected with pulmonary phthisis were only twice as numerous as the females. The percentage for males was 51·7, and for females 36·7. Heinze found a corresponding disproportion, 33·6 per cent. of the males had the larynx affected, as against 21·6 of the females.

The greater liability of the male sex to disease of the larynx is not peculiar to tuberculosis, but is found to exist for most laryngeal affections. Thus men suffer much more frequently than women from chronic laryngitis and from laryngeal growths. Males, through their occupations, are more exposed to dust and to extremes of hot and cold air, and this may partly account for the disproportion. The possible influence of smoking must also be considered. The mode of infection in most cases is undoubtedly from the lungs by means of the bacilli-laden sputum, but primary cases in which the bacillus is probably directly conveyed to the larynx through inhalation, are more common than is usually taught. It is evident that the larynx must exhibit a considerable degree of resistance, as shown by the long period in which it remains unaffected in pulmonary phthisis, although the bacillus must be constantly passing over its mucous membrane. Lake suggests that the first part of the process is a surface infection by the micrococci of the sputum, which cause a minute abscess in the epithelial layer tending to the formation of a shallow ulcer, which subsequently becomes infected by the bacilli. We know, however, that the bacilli have the power of penetrating the mucous membranes without any breach of surface, and that an erosion is not a necessary preliminary condition.

It is certain that tuberculous nodules are found in the mucous membrane previous to the existence of any apparent erosion. The tubercles are generally at first situated in the superficial layers of the mucosa just beneath the epithelium, and gradually occupy the deeper layers, although always less abundant there. These become caseous, the epithelium over them becomes necrotic, and an ulcer is formed, which gradually increases in depth and extent. The tissue in which the tubercles are deposited becomes generally thickened, so that the depth of the mucous membrane is three or four times as great as the normal.

The most common seats of tuberculous ulceration are the vocal cords, especially their posterior extremities the *processus vocales*, and the interarytenoid fold. The aryepiglottic folds frequently become swollen. The epiglottis is less frequently affected, and the ventricular bands rarely. We shall consider the various lesions separately. As regards the *cords*, a shallow superficial ulcer appears on the posterior third of the cord, most usually on its upper surface, sometimes on the internal edge. This ulcer

may spread in depth until the cartilage is reached, but often may also spread longitudinally, a not uncommon result being a splitting of the cord, producing a terrace-like arrangement. Sometimes only one cord is affected, at other times both. Sometimes there is a fleshy swelling of the whole of one cord. In the inter-arytenoid fold first there is swelling, which produces a projection between the cords, and next ulceration occurs, producing a jagged appearance from the presence of protruding granulations. Such inter-arytenoid ulceration is very characteristic. When the arytenoids are affected, there is more or less swelling, so that these often form large pyriform bodies. The epiglottis may be uniformly swollen, forming a turban-shaped mass. When ulceration occurs, this, as a rule, first appears on the laryngeal aspect. Much destruction of the epiglottis is more usual in syphilis than in tuberculosis, although more common in tubercle than is generally supposed. The ventricular bands may be considerably swollen and ulcerated, but this usually occurs late, when there is extensive general disease.

A few cases have been recorded where the tuberculous process has resulted in the formation of a definite tumour. Such tumours are usually sessile, and situated on the cords, ventricular bands or ventricles, but may occur on any part. They are of slow growth, and have been known to last for years. They consist of round-celled tissue, enclosing tubercles, sometimes with giant cells and sometimes caseous and degenerate. Tubercle bacilli are generally to be detected in them.

Symptoms.—The symptoms of laryngeal tuberculosis are alterations of the voice, pain, difficulty in swallowing, cough, dyspnœa, etc. Hoarseness or aphonia is generally the earliest of these to be noticed. Hoarseness is the more common of the two, but aphonia comes on sooner or later. Abnormal sensations in the throat are not infrequently noticeable early. These may be classed under the name paræsthesia, and consist of slight soreness, pricking, and various degrees of discomfort about the larynx. Actual pain does not generally occur until there is ulceration, and it is specially marked when the epiglottis and aryepiglottic folds have become affected. Under the same circumstances, dysphagia is usually experienced. This may simply amount to a certain degree of difficulty in swallowing, but generally there is pain on swallowing, as well as difficulty when ulceration has occurred in the situations mentioned. Dysphagia is always a grave symptom. Still more serious is the entrance of food into the trachea on swallowing. Actual dyspnœa is rare, but when it occurs is exceedingly grave, and points to the existence of stenosis of the glottis. Cough is frequent, but is not specially characteristic.

The laryngoscopic appearances will be gathered from the description already given of the morbid anatomy. A good deal of stress has been laid on the existence of marked anæmia of the larynx in the early stages. It often happens, however, that there is some congestion just at this time. When the vocal cords are affected, they are at first usually reddened and slightly swollen, and an ulcer is probably visible at the processus vocalis. When the disease is more advanced, the split or terraced appearance of the cords is very characteristic. A considerable portion of the cords may be destroyed. Ulceration in the inter-arytenoid fold, with the projecting granulations as already described, is another early affection. The pyriform swellings of the aryepiglottic folds and the turban-like swelling of the epiglottis are very characteristic of the later stages. It is not uncommon in the course of the disease to get impaired mobility of the vocal cords.

Functional paresis of the adductors is frequent at an early stage. A cord may become completely fixed from ankylosis of the corresponding crico-arytenoid joint, or it may become more or less motionless from involvement of the recurrent laryngeal.

Diagnosis.—Chronic laryngitis, syphilis, and malignant disease have to be carefully considered. Tuberculous laryngitis is sometimes taken for chronic laryngitis, especially in the early stages. The rule laid down by Morell Mackenzie, that in all cases of chronic laryngitis of some months' standing the lungs should be carefully examined, is an excellent one. The examination of the sputum in such a case is also of great importance. Limitation of chronic laryngitis to one cord is always suspicious of tuberculosis. I have seen a number of cases where it would have been impossible to have given a positive diagnosis without the aid afforded by the discovery of bacilli in the sputum. In one such case the patient had been quite recently informed by a throat specialist that his throat condition was simply catarrhal, and that his cough was due to an elongated uvula which had been promptly ablated. Finding bacilli in the sputum, I gave a different opinion. The patient died within a year from laryngeal and pulmonary tuberculosis.

There is sometimes considerable difficulty in distinguishing syphilis from tubercle of the larynx. Syphilis is, as a rule, more rapidly destructive, and ulcerations in this disease are generally larger, deeper, and fewer in number. The syphilitic ulcer is usually surrounded by a considerable amount of congestion and swelling. In all doubtful cases iodide of potassium should be tried, and careful examinations of the sputum made for bacilli. The possibility of the coexistence of tubercle and syphilis should be borne in mind.

Malignant disease, as a rule, occurs at a later period of life than that at which tuberculosis is most commonly met with. It is very rare before 40. Tumour formation is much more definite than is usual in tuberculosis, although those rare cases of tuberculous tumour already mentioned must be borne in mind. Malignant disease is more likely to be limited to one side than is tubercle, and there to be accompanied by a considerable amount of swelling. Often it is extremely difficult to distinguish the two, and frequent examinations of the sputum should be made.

Prognosis.—The prognosis in this affection is always comparatively grave, although of late years treatment has been much more successful in early and limited forms of the disease than was formerly the case. Whenever there is continued severe pain, accompanied with difficulty in swallowing, there is then practically no hope. The same is true when there is evidence of laryngeal obstruction and inspiratory dyspnœa. On the other hand, if the disease is confined to the cords or interary-tenoid fold, and the general condition is good, the pulse quiet, the appetite hearty, and the amount of disease in the lungs limited, and there is little or no fever, there is good prospect that the disease will be amenable to local and general treatment. Where the epiglottis is affected, cases seldom if ever do well. Irritability of the pharynx and larynx is always a bad sign.

Treatment.—The treatment of laryngeal tuberculosis may be divided into general and local. General treatment comprises the same measures which are recommended for pulmonary tuberculosis. Patients with laryngeal tuberculosis do not, as a rule, do well at the high altitudes. If it is thought advisable to recommend a change of air, Hastings, Bournemouth, Torquay,

Mentone, or Madeira, are among the resorts which have been found most beneficial. Dust is extremely trying to laryngeal cases. Smoking is probably injurious, and should be forbidden or strictly limited. Local treatment may be divided into palliative or symptomatic and radical, the former consisting of applications to relieve pain or diminish irritability, the latter of treatment calculated to promote the healing of lesions. We shall consider the latter first. The most important method at present employed is the application of lactic acid to the ulcerated surface. Lactic acid is employed in strengths varying from 20 per cent. up to the pure acid. It is applied on cotton-wool, which is firmly fixed on a special instrument, a laryngeal screw holder. Before applying it, the ulcerated surface may be cleansed, as recommended by Bosworth;—Dobell's solution, carbolic acid, 12 grs.; sod. bicarb., ½ drm.; glycer., 2 oz.; borax, 1 drm.; aqua ad Oj, being applied by means of an atomiser. The larynx should then be painted with a 10 per cent. solution of cocaine. Some also recommend a final application of cocaine after the lactic acid has been applied. Some begin with applications of 20 per cent., and gradually increase the strength to 50 per cent.; but Percy Kidd, who has had a very large experience at the Brompton Hospital, recommends that a beginning should be made with 50 per cent., and that after four or five sittings the pure acid should be used. It is essential that the application of the lactic acid should be thorough, that it should be well rubbed in, and that as soon as the patient has got over the effects of the first application, a second should be made. The lactic acid may be applied daily, or every two or three days.

The cases most suitable for this treatment are those in which there is little lung disease, and that not active, in which there is ulceration limited to the cords or inter-arytenoid folds, and not much swelling or general infiltration. It is very important, too, that there should be little irritability of the larynx. Where this is a marked feature, no great amount of good is to be expected from local treatment of this kind. It is not advisable to employ this treatment when there is extensive and active lung disease. Lactic acid should not be applied unless there is ulceration. Sometimes the application of lactic acid is combined with curetting or cauterising with the galvano-cautery. Curetting was recommended by Heryng of Warsaw, and both it and the application of the galvano-cautery may prove beneficial by paving the way for the acid, and enabling it earlier to reach the actively tuberculous process. The proposal to scarify and curette before actual ulceration has occurred, in order that the acid may be directly applied to the diseased tissue, has not met with approval.

Palliative treatment consists in the use of cocaine, menthol, morphine, orthoform, and iodoform. For the relief of dysphagia, cocaine is the most valuable remedy we have. It may be used in the form of lozenges, pastilles, etc., containing $\frac{1}{10}$ gr. in each, two or three of which may be taken before meals. A 2 per cent. solution may be employed in the form of a spray, which the patient may use himself before meals. Menthol may be used for the same purpose in the form of a spray, a 2 per cent. solution in olive oil being used, or twenty drops of a 20 per cent. alcoholic solution may be inhaled on a respirator. The latter solution may be applied directly to the larynx to diminish irritability. Morphine, orthoform, and iodoform may be applied by means of insufflations. Before the introduction of lactic acid, iodoform was much more frequently used than it is now. I have seen great benefit from the daily insufflation of a powder, similar to that mentioned as useful in ulceration of the tongue

or palate, consisting of finely powdered iodoform and starch, borax or boric acid, a grain each, with $\frac{1}{2}$ gr. of hydrochloride of morphine. Iodol has more recently been employed for the same purpose. When dysphagia is not relieved by these remedies, it may be necessary to feed the patient by means of a soft œsophageal tube. When there is trouble with fluids, the patient may find it easier to swallow if he lies prone on the stomach, and hangs his head over the edge of the couch or bed. When there is urgent dyspnœa, tracheotomy may be necessary.

TRACHEA AND BRONCHI.

Tracheal tubercle occurs in a considerable number of cases in the later stages of pulmonary tuberculosis, but, as far as is known, is never primary.

Usually, when the trachea is affected, the larynx is tuberculous also, but exceptionally the larynx escapes. The bronchi are less frequently involved than the trachea. That the infection has taken place through the sputum, is shown by the ulceration occurring exactly in the track which it has had to travel, the bronchus leading to the cavity in which active disease is found being affected, while the others escape. Ulceration of the trachea was found in eighty-four out of 454 fatal cases of pulmonary tuberculosis examined at the Brompton Hospital—a proportion of 20 per cent. of the male cases, and 13·5 per cent. of the females. There was bronchial ulceration in sixteen out of 382 cases.

Miliary tubercles in the trachea are seldom met with, but I have seen a few cases. Ulcers may be few and shallow, or nearly the whole interior may be ulcerated, the cartilages being exposed, and their bare extremities projecting inwards into the lumen of the tube. Sometimes the cartilages are destroyed, and the œsophagus may be perforated, subcutaneous emphysema may occur, or an abscess may form and open externally.

There are no characteristic symptoms of tracheal or bronchial ulceration which can enable us to diagnose it. This being so, nothing need be said about treatment.

LUNGS.

It required a genius like Laennec to recognise the unity of the different forms which tuberculosis assumes in the lungs. The first impression on studying the various lesions is that of inextricable confusion, and there is little wonder that, arguing from a clinical as well as a pathological standpoint, many maintained that the different forms of pulmonary tuberculosis were not merely varied types of the same disease, but were so many distinct and different diseases. This was held to be the case with regard to miliary tubercle, caseous pneumonia, and fibroid phthisis, which were considered to have little or nothing in common, although they might be met with simultaneously in the same lung.

Acute miliary tuberculosis of the lungs has already been sufficiently described. In this form of the disease the virus is disseminated through the lungs by means of the blood stream. In the forms we are now about to discuss the virus is principally sown through the medium of the air passages.

ACUTE PNEUMONIC PHTHISIS.

The acute pneumonic form of pulmonary tuberculosis is characterised by a rapid caseation of lung tissue. It may be either a primary affection, or, as more often happens, it is secondary to chronic tuberculosis of the lungs. We shall here only deal with the primary form, premising that a similar condition may supervene in a case of chronic phthisis.

Morbid anatomy.—Tracts of grey, red, or caseous consolidation of various sizes, cavities due to the softening of the centres of caseous masses, and granulations in other parts of the lungs, are the principal lesions observed with the naked eye. The grey infiltration or consolidation appears under two forms, one soft, of an ashy colour, and more or less granular on section, and another firm, glistening, semi-transparent, or with a gelatinous appearance. In both these forms there is a total absence of injection. In the red infiltration the affected tissue is hyperæmic, granular, opaque, and softer than the grey. The tissue affected with caseation looks as if infiltrated with mastic. It is yellow or greyish white, finely granular, dry, and friable, and, as in the grey consolidation, anæmic. Its vessels and bronchi can no longer be recognised, and the latter are filled with exudation. The consolidations in some cases are confluent, affecting the whole or the greater part of one lobe, as in lobar pneumonia, or they may be scattered and have a broncho-pneumonic distribution.

Excavation almost invariably arises from the softening or sloughing of caseous masses, which may or may not be associated with either red or grey infiltrations. On section small collections of pus, or cavities already formed, of various sizes, will be found in the interior of these consolidations. The walls of these abscesses or cavities are usually composed of yellow caseous matter. Smaller cavities frequently fuse together, forming one larger cavity communicating with a bronchus, or the lung may be honeycombed by a number of small intercommunicating cavities. Softening may occur immediately under the pleura, resulting in its necrosis and perforation. Generally the pleura over a superficial caseous mass becomes coated with fibrinous exudation. In the remaining portions of the lung, grey, white and yellow tubercle may be distributed as in acute miliary tuberculosis.

Bacilli may sometimes be found to be present in large number in the consolidated areas. Sections of these parts show filling of the alveoli with fibrin filaments mingled with round cells, which here and there are granular. The walls of the vessels whose lumina are obliterated, are thickened and infiltrated by small cells. Clumps of bacilli may be found, on staining in the proper manner, in the perivascular connective tissue, in the thickened vessel wall, and in some of the peripheral alveoli. The principal seat of the bacilli in lobar caseous pneumonia is at the centre of the infundibula, where the small cells are most numerous.

Emphysema is a very common result or accompaniment of the more acute forms of pulmonary tuberculosis. It is often general, affecting those parts of the lungs which are not consolidated. As a result the lungs may be very bulky. In other cases it is limited to the apices or to the free borders of the lobes. Patches of collapse are not infrequent, especially in the case of children. This form of acute pulmonary tuberculosis is often accompanied by tubercle of the pleura, or by a fibrinous exudation on the pleura, with or without effusion.

Symptoms.—The illness may commence either suddenly or gradually and insidiously. The acute onset is rare, the gradual onset is much the more usual. In exceptional cases the symptoms attending a sudden invasion may closely resemble those of acute pneumonia, with rigors, fever, and extreme prostration. Not merely the invasion, but the early period of illness, may closely simulate acute pneumonia. In other cases hæmoptysis is the earliest symptom, and fever and prostration appear later. Both rigors and hæmoptysis may recur during the course of the illness.

The symptoms attending the gradual and more usual mode of onset are vague, and are often misunderstood. The patient is perhaps thought to be suffering from bronchial catarrh, from the effects of an attack of influenza, from rheumatism, or from dyspepsia. The patient feels weak and languid, loses appetite, suffers from chilliness and aching of the limbs, and probably bronchial catarrh. The temperature, if taken, is found to be febrile. Cough is seldom absent for long. In some cases gastric symptoms predominate, and the main features of the cases may be dyspepsia, with discomfort or actual pain after food, more or less complete loss of appetite, constipation, and sometimes vomiting and diarrhœa. Whether the onset is acute or gradual, the later symptoms are the same.

Physical signs.—These will vary according as there are scattered patches of consolidation of a broncho-pneumonic type, or a considerable extent of consolidation affecting one or more lobes. As bronchial catarrh is frequently present, rhonchi may be audible generally over the lungs. In the areas affected by consolidation, the usual physical signs of this condition—bronchial breathing, bronchophony, and increased vocal fremitus and resonance—will be present. Râles may or may not be present over the consolidated area. It is significant of these cases that the physical signs persist in the situation where they first appear, although other parts are successively affected.

The fever is usually high, the evening temperatures reaching from 103° to 105° F. It may be nearly continuous, or assume a remittent type, and become very irregular. The pulse rate is variable; it may be rapid, or it may not exceed 80 in the minute. The respirations are quick, ranging from 20 to 40 in the minute, but they are seldom so rapid in proportion to the pulse as in acute pneumonia. There is generally some dyspnœa, but often not to such an extent as to be distressing to the patient. A certain degree of cyanosis is not unusual, but is less marked than in the pulmonary form of acute miliary tuberculosis. . Cough may be slight or frequent and troublesome, and the expectoration may be scanty throughout or abundant. The sputa may be rusty throughout, or may consist almost entirely of blood. In other cases they are mucous at first, later becoming purulent. In the latter stage, elastic fibres are generally to be found. Bacilli are almost always present. Gangrene is not infrequent as a terminal process, and may impart its characteristic odour to the sputa.

The appetite is usually in abeyance from the first. The tongue probably becomes thickly coated. The bowels may be constipated or loose. The body rapidly emaciates, and prostration becomes more marked as the disease progresses. Profuse sweating is not uncommon. Delirium, restlessness, and insomnia at night are frequent symptoms. Albuminuria is not uncommon. The spleen is often moderately enlarged.

Course.—The course of the disease varies in duration. Exceptional cases terminate in ten days or a fortnight, some last two to three months,

and others are even more protracted. Death usually ensues from asthenia and prostration, or from some complication, such as hæmoptysis. The patient may be quite conscious to the end. It must be remembered that cases, which to begin with are acute, not very infrequently pass into a chronic condition, and may subsequently undergo arrest.

Diagnosis and prognosis.—When the invasion is sudden, a case of acute phthisis at the outset may be mistaken for ordinary acute pneumonia, and it is perhaps the protracted course which first excites suspicion that it is anything different. I do not know that it is possible to make a diagnosis in this type at quite an early stage. Even where there is evidence of previous tubercle, it must be impossible to exclude ordinary pneumonia occurring in a tuberculous subject. The persistence of the fever, and the gradual extension of the consolidation to other parts, without clearing up in the parts first affected, are important points. The examination of the sputum for tubercle bacilli and elastic tissue will help to clear up the diagnosis. Empyema following on pneumonia may be mistaken for tuberculosis, but in this case there is generally a crisis at the usual time, and a gradual return of the fever later on. Whenever there are signs of fluid, an exploratory puncture should be made. Influenza is another malady for which acute pulmonary phthisis may be mistaken, but in this case the mistake can only be made at the beginning. As a rule, the disease proceeds to a fatal termination. In rare cases, as has been mentioned, it passes into a chronic condition, and becomes one of ordinary chronic phthisis.

Treatment.—The patient should be kept at rest in bed in a well-ventilated room. The food should be abundant, and adapted to the condition of the patient's digestion. Symptoms must be treated as they arise. For details as to treatment, reference must be made to the following section on chronic pulmonary tuberculosis.

CHRONIC PULMONARY TUBERCULOSIS.

Morbid anatomy.—In chronic pulmonary tuberculosis or phthisis pulmonalis the essential character of the lesions is fibrosis. We have seen how the miliary tubercle may undergo a fibrous change quite independently of caseation, and also how, while the centre may caseate, the outer part of a tubercle may become fibrous. In all cases of chronic phthisis there is evidence of the fibrous change, but the actual chronic lesions at the post-mortem are very often mingled with more recent morbid processes.

The disease is nearly always oldest and most advanced at the apices of the upper lobes. When the lower lobes are affected, their apices similarly are, as a rule, the most early to be involved. The disease is usually bilateral, although one lung often shows older and more extensive disease than the other. Cavities are almost invariably present. These are often of a large size. Sometimes a whole lobe, and, in rare cases, nearly an entire lung, may be destroyed. The commonest situation for excavation is in the upper half of the upper lobe. It is not at all infrequent for it to occur in the lower lobe, near its apex. Cavities may be quite superficial, or they may be separated from the surface by lung tissue affected with fibrosis, or otherwise diseased. The cavities may be rounded in shape or ramifying, multilocular, and extremely irregular. Their walls may be smooth and fibrous, and lined with a pyogenic membrane, or, when the cavities are

recent, their walls may be irregular, and composed of softening caseous material. Very frequently they are traversed by trabeculæ formed of the thickened remains of fibrous septa and of obliterated vessels. Such trabeculæ may course across the walls, or run through the interior of the cavities.

Cavities nearly always at the autopsy contain more or less purulent secretion, but we have evidence that during life perfectly dry cavities may exist. Indurated tissue, as a rule, surrounds the chronic cavities. Such tissue is grey, dense, and glistening, and frequently embedded in it are tubercles either fibrous or caseous. Fibrosis, however, is not an uncommon change independently of excavation. It is not unusual when making post-mortem examinations on persons dead from accident or other causes, to find masses of induration at one or other apex. These on being cut into are seen to contain in their interior, dry caseous material, or cretaceous nodules, or both, surrounding which are strands of dense pigmented fibrous tissue. Such indurated patches are frequently observed at the apices of the lungs, in cases where more active disease occurs below.

In these cases there may also be found patches of consolidation resembling the grey infiltration of acute pneumonic phthisis. These are firm, smooth, and glistening, and tough to cut. Caseous nodules, firm or softened, may be embedded in the infiltration. Various forms of granulation may be irregularly distributed throughout the lungs. These are often grouped in a racemose fashion. They are firm and tough, as a rule deeply pigmented, and surrounded by fibrous tissue. Superimposed on these older lesions, any of those met with in acute pneumonic phthisis or in acute miliary tuberculosis may be found. Dilatations of the bronchi are frequent in connection with tuberculous lesions. They are most common in chronic cases where fibrosis is a predominating feature, but they may occur even in acute cases. The dilatations are usually fusiform. Less commonly the dilated bronchus terminates in a globular expansion, but it is difficult to distinguish bronchiectatic cavities from those which have formed in the ordinary way. In the ordinary cavity the edge of the bronchus opening into it is sharply truncated, and its mucous membrane is swollen. When the cavity is of old standing, this distinction may disappear.

In chronic phthisis, emphysema is frequently met with surrounding indurated patches, or along the borders of the lobes, or in other situations, the bases in particular, where there is neither excavation nor consolidation. The emphysema in such cases is not uncommonly of the atrophic type.

The pleura is nearly always involved in the course of the disease. Adhesions are almost invariable. Sometimes the lung becomes everywhere united to the parietes. Sometimes the adhesions are limited to the apex. In the latter situation, the pleura may become much thickened, forming a layer from a quarter to half an inch thick. On section it may be dense and fibrous or œdematous-looking. Fibrinous exudations will be present where there are more recent superficial consolidations. Effusions are not uncommon at one or both bases. Aneurysms of branches of the pulmonary artery are very frequent in cases of profuse hæmoptysis, their rupture being by far the most usual cause of this event. They are easily overlooked, and sometimes are only discovered after carefully cutting up the lungs piece by piece. In size, they vary from a small pea to a walnut, the latter size, however, being very exceptional. They are not uncommonly multiple, and a dozen or more may be present in one case. The aneurysms

may be met with on the walls of large cavities, but it is more common to find them in medium-sized vomicæ, and occasionally they occur as round pedunculated tumours, lying in cavities little bigger than themselves. They sometimes form in connection with quite small branches of the pulmonary artery. The mode of production of these aneurysms is the same as that of septic aneurysms elsewhere. First, there is an inflammatory process in the wall of the vessel, a suppurative arteritis, by which the middle coat is destroyed. The vessel then gradually dilates, and the outer and inner coats become expanded, the former at the pedicle being continuous with the wall of the cavity. The bronchial glands are very frequently tuberculous in pulmonary tuberculosis. In acute cases, one or more are generally caseous; in chronic cases, a fibroid or calcareous condition is not at all uncommon. The larynx and intestines are very often secondarily affected. These and other concomitant tuberculous complications have been already fully described under special headings.

Arrested tuberculosis.—Everyone who has much experience in post-mortem examinations must be struck with the comparative frequency of evidences of healed tubercle unexpectedly found in persons who have died from other causes. The most usual lesions met with are fibrous, calcareous, or cheesy masses, embedded in the apices of the lungs, to which allusion has already been made, and calcareous or fibrous and pigmented bronchial or mesenteric glands. The relative frequency of such lesions has been variously estimated: Heitler of Vienna, 16,562 autopsies, 4 per cent.; Osler, 1000 autopsies, 7·5 per cent.; Fowler, 1943 autopsies, 9 per cent.; Sidney Martin, 445 autopsies, 9·4 per cent.; Coats, 103 autopsies, 23 per cent. Such lesions are very frequently met with in patients dying from chronic pulmonary tuberculosis.

Associated lesions.—*Digestive system.*—The morbid changes in the stomach are chiefly of a catarrhal nature affecting the glandular structure, and accompanied by general thickening of the mucous membrane. Rarely, simple ulcers have been found, but it is doubtful whether the association is other than accidental.

The intestinal tract is similarly likely to be affected with catarrh, and simple as well as tuberculous ulcers may be present. In the large intestine sloughing of the mucous membrane, and the formation of a croupous false membrane, sometimes occurs. Amyloid degeneration of the intestinal mucous membrane is not infrequently observed in chronic cases, and the stomach occasionally is similarly affected.

Fistula in ano, and its connection with tuberculosis, has been already discussed.

Decided fatty degeneration of the liver is met with in about 30 per cent. of the cases. The organ, as usual, is enlarged, pale, anæmic, greasy, and abnormally soft and friable. Amyloid degeneration of the liver occurs in about 10 per cent. of the cases. Chronic congestion or nutmeg liver is rare. Cirrhosis is too commonly associated with tubercle for this to be merely accidental. In such cases there is nearly always a history of alcohol, which, while directly causing the cirrhosis, has probably predisposed to tubercle.

The pancreas, as a rule, shows no characteristic change.

The spleen in the more acute cases is often enlarged and softened. Amyloid degeneration is more common in the spleen than in the liver, and may occur in the diffuse, or in the sago form. In the diffuse form, the organ may be considerably enlarged, and very firm and heavy, the greater part of

the tissue being affected; in the sago form, the degeneration is limited to the Malpighian bodies.

The heart is generally small, but is less diminished in size than in some other wasting diseases. The atrophy, as a rule, affects both sides equally, but the right side may be dilated, especially in very chronic cases. The muscle is pale, and under the microscope may show brown atrophy, or a certain amount of fatty degeneration. While mitral stenosis is rare, other forms of valvular lesion are probably neither more nor less frequent than they are in the case of other diseases. Congenital disease of the heart is often associated with pulmonary tuberculosis.

Thrombosis of the popliteal, femoral, or other veins is a not uncommon occurrence, commencing a week or two before the fatal termination of a case of phthisis. Thrombosis, although more frequent towards the end, may occur at an earlier stage and be recovered from.

Genito-urinary system.—Amyloid disease of the kidneys is a common result of chronic phthisis. As to what its actual frequency is, very different estimates have been given. In many cases where examination with the naked eye, after staining the section with iodine, shows nothing abnormal, microscopic examination, after staining with methyl-violet, methylene-blue, or methyl-green, reveals the presence of amyloid change in the glomeruli. Congestion and chronic interstitial nephritis are among the other changes met with. No changes, other than tuberculous, are likely to be found in the bladder or genital organs.

The *nervous system* shows no characteristic lesion independent of tubercle.

Symptoms.—The usual symptoms of pulmonary tuberculosis are cough and expectoration, emaciation, fever, sweating at night, loss of appetite and dyspepsia, shortness of breath, and, probably at some period of the disease, hæmoptysis. The lesions in the lungs generally give rise to characteristic physical signs, as already observed. The older descriptions divided the illness into three stages. In the first stage there was simply the deposit of tubercle; in the second, there was consolidation and softening; and in the third, cavities had formed. While, however, one part of the lung may be in one stage, another part is in another. No useful purpose is served by giving separate descriptions of the symptoms in different stages. The disease may be arrested at any stage, and the patient with cavities in his lungs is frequently much less ill, and has better prospects of life, than when the morbid process has not yet reached the cavity stage.

The mode of onset of chronic pulmonary tuberculosis is, as a rule, very insidious. The patient gets out of health, loses his appetite, is easily tired, finds himself short of breath, and probably has a cough, with mucous expectoration. If the temperature be taken, it will likely be found to be up in the afternoon or evening. Sometimes hæmoptysis is apparently the first symptom, although on investigation it will generally be found that the patient has been out of health before. In other cases, the illness commences with pleurisy. Sometimes the patient first consults the doctor on account of hoarseness.

Sometimes during the onset, pulmonary and larnygeal symptoms are conspicuous by their absence. This is not uncommonly the case with old people and children. In these cases, there is failure of health without obvious cause. The patient complains of weakness, lassitude, and loss of flesh, and probably if his temperature be taken there will be found to be some fever. Gastric derangement is not an infrequent symptom at the

onset. It shows itself in the form of atonic dyspepsia, with a red or furred tongue, pain after food, anorexia, and sometimes vomiting. Amenorrhœa in females and anæmia are other common symptoms of the early stage. We shall now proceed to describe the principal symptoms in detail.

Cough.—Cough is one of the earliest as well as one of the most persistent symptoms. In the early stages it is often short, dry, and hacking, occurring principally in the morning and evening. Later it often becomes noisy, paroxysmal, and distressing. Sometimes the cough is excited by food, and after a meal may be so severe as to be terminated by vomiting. It often becomes more frequent and more distressing as the disease advances. It is apt to be aggravated by excitement or exertion.

Sputum.—If there is any expectoration in the early stages, it is probably simply mucus with perhaps carbon particles. It next becomes muco-purulent, with greenish or yellowish streaks, and later, thicker and more tenacious, while a greenish yellow tinge pervades the whole. Frequently the sputa acquire a nummulated shape. The quantity of the expectoration in the twenty-four hours varies from a drachm to 6 or 10 oz., or even more. Analysis has shown that the sputa contain 94 per cent. of water, together with mucin, extractives, albumin, fat, and inorganic matter consisting of chloride of sodium and phosphates. They have a faint sweetish odour, but ordinarily no fœtor. Occasionally calcareous masses are expectorated. These point to the existence of an old cured lesion. Such calcareous masses are not unfrequently found embedded in the lung at the centre of such obsolete tuberculous nodules. They vary in size from a coriander to a cherry stone. As many as five hundred have been known to be expectorated in an individual case. In a cover-glass specimen of sputum may be seen epithelial cells from the mucous membrane and the pulmonary alveoli, leucocytes, and fatty débris. Importance has been attached by Teichmuller to eosinophile cells, their presence being considered by him a favourable sign, while their rapid disappearance or persistent absence is of bad omen.

Bacilli.—The presence of the tubercle bacillus is the only really characteristic feature of the sputum of pulmonary tuberculosis. It is never found in any expectoration, except that from a phthisical patient. It is not always to be found in phthisis, but if, after several examinations of the sputum by an experienced observer, no bacilli are found, it is very unlikely that the case is one of active tuberculosis. The mode of examining sputum for bacilli has already been described.

While the presence of the bacilli in the sputum has a very important diagnostic value, little help in prognosis is afforded by repeated examinations. Changes in the appearances of the bacilli are of no moment, and differences in their number do not help. The disappearance of bacilli from the sputum, however, over a certain period of time is of great importance, and if associated with favourable symptoms points to arrest of the disease. When examinations are made, the patient himself should, as a rule, not be informed of their results. If the bacilli are few, he is apt to be unduly elated; if they are many, to be unnecessarily depressed. Better there should be no examinations at all, after the first for diagnostic purposes, than that a morbid anxiety regarding bacilli should be created and fostered.

Elastic fibres.—The presence of elastic fibres in the sputum is only second in importance to that of the bacilli. Their presence shows that

softening is in progress. The fibres are short and narrow, with wavy outline and double contour. An alveolar arrangement of the fibres is a great help to diagnosis. The fibres resist the action of acetic acid. By heating the sputum, till it boils, with an equal amount of a solution of caustic soda, 20 grs. to the ounce, allowing this to stand, and examining the deposit, as recommended by Fenwick, the fibres are most readily discovered.

Care should be taken not to mistake foreign bodies, such as fibres of wool, cotton, or vegetable substances accidentally present, for elastic tissue. It is advisable to use a silk cloth for wiping slides and cover-glasses, when examining for elastic tissue.

Hæmoptysis is a very important symptom, not simply on account of its frequency, but because its occurrence is very strong presumptive evidence of the existence of tubercles. It may occur at any stage of the disease. In a considerable proportion of cases, it is an early symptom, sometimes the earliest. It may be the immediate cause of death. In probably about three-fourths of all cases of chronic pulmonary tuberculosis, hæmoptysis occurs during some period of the illness.

Among my hospital out-patients, I found a history of hæmoptysis in about 45 per cent. of the phthisical. Thus, out of 1670 phthisical patients, in 742 hæmoptysis occurred, either before or during their period of attendance. In about a sixth of the whole number of cases, the hæmorrhage was a large one; in about a fifth, it was a small amount; and in the remaining fraction, consisting of about a twelfth of the whole, it only amounted to streaks of blood in the sputum. Reginald Thompson states that out of 5000 cases of well-marked pulmonary disease among his out-patients, in 45 per cent. hæmorrhage of a decided kind occurred. Pollock gives a percentage of 58·4, founded on an experience of 1200 out-patient cases, and C. T. Williams out of 1000 private cases found 569 affected with bleeding, or 57 per cent. My experience is, that hæmoptysis is considerably more frequent in the male sex than in the female, and this is not explained by the larger number of male cases of phthisis that one sees. A larger proportion of males relatively have hæmoptysis. Thus 49 per cent. of my male cases spat blood, while only 39 per cent. of the females were so affected. Pollock found that of 351 cases of profuse hæmoptysis, 267 were males, 84 females.

Hæmoptysis is comparatively rare at the two extremes of life, children and old people being relatively less subject to it. Occasionally, however, they may have large hæmorrhages. Hæmoptysis appears from statistics to be more frequent during the summer months than at other times of the year. Hæmoptysis, as has been pointed out, may be the first obvious symptom of the disease. On the whole it is more frequent in the later stages. Very often the patient suffers from several attacks in the course of his illness. Care must be taken to distinguish between hæmoptysis on the one hand, and epistaxis, bleeding from the gums and fauces, etc., and hæmatemesis on the other.

Sometimes the patient thinks he can feel the blood coming from a particular part of the lungs, but such sensations cannot be depended on. The blood brought up from the lungs is nearly always bright and frothy, and is fluid and not clotted. In this way it contrasts with blood from the stomach, which is either a dark grumous fluid, like coffee-grounds, or may be partly composed of clots. A large quantity may come up at once or, as more frequently happens, a number of separate mouthfuls are brought up. Although hæmoptysis usually subsides within a short time, cases occur where the patient continues to bring up quantities of blood for days

together. The sputa are generally stained for some days after the first bleeding has occurred. This is a point of great importance, as distinguishing from hæmatemesis.

At the Brompton Hospital, one out of every thirteen or fourteen deaths is from hæmoptysis. Out of 915 deaths from pulmonary tuberculosis, there were sixty-six from hæmorrhage, giving a proportion of 7·2 per cent. In two-thirds of the cases, pulmonary aneurysms were found. Hospital experience must necessarily place the death rate from hæmoptysis too high. Cases with hæmoptysis are admitted on account of urgency, and therefore are present beyond their normal proportion. In the case of a hospital which admitted hæmoptysis cases, but not ordinary phthisical cases, it would appear that nearly every patient with phthisis died from hæmoptysis—a *reductio ad absurdum.* West's estimate of less than 3 per cent. is probably correct.

Shortness of breath is a very constant accompaniment of pulmonary tuberculosis. It is seldom, unless from some complication, that it amounts to actual dyspnœa. Ordinarily it is only experienced on exertion, when the patient mounts a stair, or walks on rising ground. As long as he is at rest or on level ground he remains unembarrassed in his breathing. But although the patient may be unconscious of it, often the physician will observe the breathing is more rapid than normal. Cyanosis is a very unusual phenomenon, except in advanced cases, and in cases where there is extensive basic disease.

Emaciation.—Wasting of the body has been looked on as the most characteristic feature of the malady, as shown by the names consumption and phthisis. It is nearly always present, and progresses as the disease advances. In very chronic cases, the patient may continue well nourished or put on weight, even while the symptoms show that the disease is active. Such cases are very exceptional. Under treatment, hygienic, climatic, and medicinal, the patient in favourable cases steadily puts on weight. When the disease is arrested, the patient may attain a greater bodily weight than at any previous time of his life.

Loss of strength and energy usually accompanies loss of weight in the progress of the disease. Lassitude is often most noticeable when the patient wakes in the morning, and it is a common complaint that he feels more tired then than when he went to bed.

Pain is not a very characteristic symptom, and when present is usually caused by involvement of the pleura. The patient may complain of pain in the side, or in the region of the clavicle, or in the scapular region. Muscular pains over the lower ribs may result from cough. There is often tenderness to percussion on the affected side, especially in the case of women.

Indigestion.—Functional disturbances of the digestive system are among the most constant and important of the symptoms unconnected with the respiratory tract. Loss of appetite is frequent at an early stage. Generally, there is a distaste for all kinds of food, but especially for fats. The patient complains of a feeling of weight and discomfort after a meal, and is likely troubled with acid eructations. A red line on the margin of the gums is not unusual, but has no special significance. The tongue, in most cases, is fairly clean, or pale and only slightly furred. In the later stages it may be thickly coated, and the mouth and throat feel dry and sticky, especially in the morning. Vomiting is a common symptom, especially among women and in the early stages. As a rule, it only occurs

after meals, and may then be preceded by a fit of coughing. It is more common after the evening meal than after the morning. The vomiting produced in this way probably depends on an abnormal reflex excitability of the gastric fibres of the vagus. In the early stages, constipation is more frequent than regularity of the bowels or diarrhœa. Diarrhœa usually occurs late, from ulceration or catarrh of the intestine. We have already referred to the gastric form of onset of the disease.

Fever.—Rise of temperature is a constant accompaniment of tubercle in its active stages. Much study has been devoted to the types of pyrexia in pulmonary tuberculosis. The numerous classes which have been described may with advantage be reduced to two: (1) Where the morning temperature is normal or subnormal and there is slight or more marked evening pyrexia; (2) where there is more or less constant pyrexia, but with evening temperatures distinctly higher than the morning.

The highest temperature is usually met with about 6 or 8 P.M., then there is a gradual fall until the lowest temperature is reached between 6 or 8 A.M., after which it gradually rises again. There is no exact regularity as to the time of the highest and lowest temperatures. The highest temperature reached, as a rule, does not exceed 103°, but rarely it may be 104°, and very rarely 105°. The lowest temperature may be normal or subnormal. The remissions or differences between the highest and lowest temperatures, in mild cases, do not amount to more than 1° or 2°, but in severe cases may be as much as 4° or 5°, or even more. *Cæteris paribus*, the high temperatures with marked remissions are met with in cases where the disease is active and advancing, and caseation a prominent feature. With quiescence of the disease, the fever may entirely disappear. Its return after disappearance is a bad sign, and points to extension and renewed activity of the disease. Fever of a continuous type, with little difference between morning and evening temperature, generally points to miliary infiltration.

Exertion and excitement are apt to temporarily increase the pyrexia. Accidental causes may also interrupt the regularity of a temperature chart, even when a patient is confined to bed. It should be remembered that although higher evening temperatures are the rule, sometimes an inverse type is met with in which the morning temperatures are the higher. This inverse type, like the continuous type, as a rule, points to miliary infiltration. As observed by Traube, intermitting fever may so characterise pulmonary tuberculosis that it may be mistaken for malaria. There may then be definite rigors, which may also occur in other cases. Osler remarks that in Philadelphia and Baltimore, where ague prevails, scores of cases of early tuberculosis are treated every year for ague.

Sweating at night is a very usual and characteristic symptom. It commonly occurs towards the early morning, when the patient may wake up bathed in perspiration. It is usually accompanied, in febrile cases, with a decided fall of temperature. It generally points to activity and progress of the disease, and as a rule disappears with cessation of fever and arrest of the disease. Profuse sweats are very exhausting as well as a source of great discomfort to the patient. Pityriasis versicolor may often be noticed among hospital patients, and is probably connected with too infrequent change of underclothing and too few ablutions. The so-called chloasma phthisicorum is decidedly rare. A slight degree of clubbing of the fingers is not uncommon in chronic cases, but one seldom sees extreme degrees of this condition, such as are met with in bronchiectasis, etc.

Pulse-rate.—This is one of the best guides to the condition of the patient. The pulse is rapid when the disease is active and progressive. It quietens down again when the disease becomes arrested. The rate of the pulse bears no necessary relation to the temperature. It may be as rapid in the morning when the temperature is nearly normal as it is in the evening when there is fever. In the later stages the pulse becomes weak as well -as rapid, and this combination is a bad sign.

The blood.—No special changes are observed in the blood. The red corpuscles are diminished in number, and are deficient in hæmoglobin. The blood platelets are increased in number, but this is by no means a peculiarity of tuberculosis

Urinary symptoms.—There are no special urinary symptoms unless the kidneys themselves become diseased. Amyloid disease is not uncommon in the later stages, and then the urine contains albumin and perhaps a very few tube casts. Albuminuria may also occur simply as the result of fever. The symptoms present when tubercle affects the urinary tract are described under a special heading. In the case of females, when phthisis attacks at the age of puberty, the onset of menstruation may be indefinitely delayed. The catamenia are frequently, sooner or later, suspended during the course of phthisis, and before complete arrest generally become irregular either in time or quantity. The presence of phthisis does not appear to interfere with impregnation. Phthisical women, indeed, seem to be quite as fertile as the non-phthisical.

It would be needless to say that the sexual appetite is diminished *pari passu* with the failure in health, if it were not that a false impression to the contrary has prevailed. Louis wrote very sensibly in regard to this point: "Presque tous ceux aux quels j'ai demandé si leur penchant a l'amour était plus développé qu'en bonne santé, indiquaient par leurs réponses que la question leur paraissait pour ainsi dire ridicule."

Nervous symptoms.—The hopefulness which hardly ever leaves the patient, until death closes the scene, is quite characteristic of the disease. It is seldom, even in the last stages, that the patient recognises how ill he is. Almost dying patients are constantly being brought to the hospital, firmly imbued with the belief that if they are only admitted they will be well in a short time. The mental faculties as a rule remain unimpaired to the end. Occasionally insanity complicates phthisis, but it has not been shown that more than the average number of phthisical patients become insane.

Symptoms of peripheral neuritis have sometimes been observed. That neuritis may be produced by tuberculosis is undoubted, but I have never myself seen it associated with tubercle, except when there was a history of drink. In nearly all the fatal cases of alcoholic neuritis, pulmonary tubercle has been found. In non-alcoholic cases, the cause of the neuritis is the toxine produced by the bacillus, and not the bacillus itself. Meningitis or tuberculous tumour in the brain will give rise to special symptoms, which are elsewhere described. Generally these complications carry the patient quickly off.

Physical signs.—The chief physical signs met with in chronic pulmonary tuberculosis are those of consolidation, softening, and excavation.

In early cases, the physical signs may afford but little help in diagnosis, and more dependence has to be placed on symptoms and on examinations of the sputum. The mere presence of miliary tubercle does not alter the resonance of the percussion note, nor does it necessarily give rise to any

abnormal auscultatory signs. It is useful to bear in mind that commonly the earlier formations of tubercle occur in the upper parts of the upper lobes, and that later the disease is nearly always more advanced about the apices. Although both lungs are usually affected, it is very seldom that they are equally so, and for a long time the amount of disease in the sounder lung may not be sufficient to produce signs of its presence.

A good deal of importance, as an early sign, has been attached to a wavy interrupted character of the inspiratory breath sounds over a localised area. Such breath sounds are not uncommonly audible over the second intercostal space near the sternum in early cases. It is probable that the presence of tubercle, acting as an obstacle to the entrance of air into the affected part at the same time as into the rest of the lung, causes the inspiratory sound to be broken up. Wavy breathing, when general, has no special significance, and when localised it may depend on various other conditions besides tubercle.

From the deficient entry of air to the affected part of the lung, there may be enfeeblement of the breath sounds, but the existence of consolidation often generally leads to a harsh or bronchial quality. The earliest physical sign which is really characteristic, is the presence of râles or crepitations. At first, crepitations may be only occasionally heard, perhaps only during the inspirations immediately following cough. Such crepitations resemble fine crackles. Care must be taken not to mistake for crepitations sounds produced in the œsophagus by the patient swallowing after coughing. This error can be avoided by telling the patient not to swallow after the cough, or by requesting him to keep his mouth open, when swallowing becomes impossible.

Comparative dulness at one or other apex is often an early physical sign, sometimes preceding crepitation. Taken in connection with other signs, even slight loss of resonance has great importance. It must be borne in mind, however, that even in health there is a slight difference between the percussion notes at the two apices, there often being a little less resonance at the right than that at the left apex. Dulness results from consolidation of lung and to some extent when there is much thickening of the pleura. In cases where the consolidation is extensive, the dulness will be so also. When the general health is good, and there is no evidence of active disease, marked dulness generally points to fibrosis of the lung.

When a portion of lung is consolidated, and the tubes leading to and permeating it are patent, the breath sounds acquire a bronchial or tubular character. The patent tubes surrounded by solid lung conduct the breath sounds from the larger tubes with great distinctness, and as no air enters the affected part, the vesicular character of the breath sounds ordinarily audible over it is completely lost. If, however, there is much thickening of pleura and narrowing or blocking of the tubes in the consolidated part of the lung, the breath sounds, instead of being tubular, may be enfeebled or almost absent. The changes in the breath sounds which occur on the formation of a cavity will be considered later. When the breath sounds are bronchial, pectoriloquy will be audible. Pectoriloquy, indeed, may often be heard before bronchial breathing. It is less easily missed than bronchial breathing, and its presence at a particular spot may lead to the detection of other signs previously overlooked. The vocal fremitus and resonance are increased over consolidated areas, except when there is much thickening of the pleura or blocking of the tubes.

When there is consolidation, and the tubes connected with the con-

solidated areas are patent, any crepitations produced will be conducted to the ear with increased distinctness, for the same reason that the breath sounds are bronchial. Such crepitations are sometimes spoken of as "consonating," and have a peculiar bright or clear quality.

The most conclusive sign of softening is the discovery of elastic tissue in the sputa. Coarse and very abundant râles with a metallic quality, succeeding râles of a dry or finely crackling quality, are generally regarded as characteristic of softening and cavity formation. No doubt in the great majority of cases it is so, but in exceptional cases such sounds may depend on other causes.

Where a portion of the lung is consolidated and air does not enter it, the corresponding part of the chest wall is comparatively motionless. A diminution or absence of movement of the region above or below the clavicle is very significant, and often at once attracts attention to the affected part. When pleurisy is a complication, friction or the usual signs of pleural effusion will be present.

The signs of a cavity.—It often happens that a cavity may be present and yet not give rise to characteristic signs. It may be deeply situated, or it may be surrounded by thickened pleura, fibrous tissue, or consolidated lung, or it may be filled with secretion, and so the ordinary signs may be modified. Moreover, the cavity must have attained a certain magnitude before its signs become well marked. The most characteristic physical signs of a cavity result from the vibration of the air in its interior in a definite way, depending on its shape and size. Both the percussion note and the sounds produced inside the cavity take on a peculiar quality, due to this cause. The pitch of the percussion note varies with the size of the cavity, being high when the cavity is small, and relatively low when it is large. The peculiar cavernous quality of the percussion note is always better elicited when the patient keeps his mouth open during the percussion. The more superficial the cavity, the more distinctly is this quality obtained. The note may then be spoken of as the cavernous percussion note. When a cavity is filled with secretion, the percussion note is simply dull.

The percussion note over a cavity sometimes possesses another peculiar quality, the well-known cracked pot sound or *bruit de pot fêlé*. It is advisable for its production that the percussion stroke should be rather sudden, but not necessarily forcible, and that the patient should keep his mouth open. In children the *pot fêlé* sound has sometimes no significance, and may be produced without there being any pathological condition. The breath sounds audible over a cavity are frequently as characteristic as the percussion. They are bronchial or tubular, with the important addition of a peculiar blowing quality due to resonance in the cavity. They become possessed of the qualities of the cavity note. These breath sounds are spoken of as cavernous or amphoric. It has been pointed out that the expiratory sound is often of a lower pitch than the inspiratory. Crepitations as well as voice and cough sounds audible over a cavity are often possessed of a similar metallic or hollow quality.

Mention should also be made of what has been called the post-tussive suction sound. After the patient coughs, in which act a certain amount of air may be expelled from the cavity, the air may be heard to return with a peculiar sucking or hissing sound, as it does when an indiarubber ball with a hole in it is compressed and suddenly allowed to expand. The presence of this sound, though characteristic, is exceptional.

We have referred to the impairment or loss of movement of the chest wall observed in consolidation of the lung. This is equally the case when there is a contracting excavation of the lung, in which case the chest wall often becomes flattened, and a hollow may form above or below the clavicle. The most striking changes occur when there is extensive loss of substance and contraction of the lung as the result of excavation or fibrosis. When such contraction occurs in the left lung, the heart is uncovered and drawn over further to the left, and its pulsations may be seen in the second and third interspaces, while the impulse may be visible as far to the left as the anterior axillary line or even further out. When the disease exists in the right lung, then there may be drawing over of the heart to the right, and pulsation of the aorta may be distinctly visible in the second right interspace. In these cases the opposite lung is generally over expanded, and reaches for some distance across the middle line.

The course of chronic pulmonary tuberculosis may be extremely protracted. The disease may be arrested at one or other stage, and no further change occur for years. In many cases arrest is only temporary. After an interval the disease once more becomes active, possibly to be again arrested later on. The extension of the disease to the larynx or intestine, or the outbreak of general tuberculosis, will bring the case to a more rapid termination than otherwise. Hæmoptysis and pneumothorax may complicate the case at any time, and prove the direct cause of death. Hæmoptysis has already been discussed at some length. It remains to say a few words regarding pneumothorax

Pneumothorax, as has been said, is a complication which may occur at almost any stage in the disease. It is not likely, however, to happen unless the morbid process is active. Its most usual cause is the undermining of the pleura by a small superficial patch of tuberculous softening.

Its onset is generally accompanied by pain in the side, dyspnœa, and more or less collapse. On examination, the affected side is found to move little and to be over-resonant the breath sounds are feeble, and possibly metallic and cavernous in character, while adventitious sounds acquire the same metallic quality. There is displacement of organs to the sound side, away from the pneumothorax. A very characteristic sign is the *bruit d'airain*, the bell sound audible over a pneumothorax on auscultation while percussion is made with two coins, one being used as pleximeter, the other as plexor. The pathognomonic succussion splash, for the eliciting of which there must be fluid as well as air in the pleura, requires that the ear or stethoscope should be applied to the chest while the patient is shaken or shakes himself. An occasional difficulty in diagnosis is to distinguish a large cavity from a pneumothorax. The direction of the displacement of organs is a very important element in the diagnosis, the displacement being towards a cavity, but away from a pneumothorax. The *bruit d'airain*, when present, points to pneumothorax rather than to pulmonary excavation.

Prognosis.—The prognosis in chronic pulmonary tuberculosis is often a matter of the highest difficulty. Some patients exhibit a surprising recuperative power, some suddenly and rapidly go down-hill, and others are unexpectedly carried off by fatal hæmoptysis, pneumothorax, or general tuberculosis. Whenever there is evidence of great activity of the disease, as shown by rapid loss of flesh and strength, profuse sweating, high temperatures, rapid cardiac action, diarrhœa, etc., the prognosis is very grave. The

complication with laryngeal tuberculosis is always very unfavourable, with the reservations already alluded to.

It must be clearly borne in mind that more depends on the general condition of the patient than on the extent or stage of the disease in the lungs as revealed by physical examination. The student, and indeed the practitioner, is apt to think that prognosis is chiefly influenced by the stage which the disease has reached in the lung. A patient in the third stage is accordingly thought to be worse than one in the second stage, and much worse than one in the first. Such an idea is an entirely erroneous one. In whatever stage the disease in the lung exists, provided the state of nutrition is good, the pulse quiet, the temperature normal, the tongue clean, the appetite hearty, and the bowels regular, the prognosis will be favourable, the more so, of course, the less the amount of the damage to the lungs. Where the reverse conditions prevail, the prognosis will be correspondingly unfavourable. We shall consider, separately, a number of side issues which affect our prognosis.

Age.—The time of life at which the disease exhibits greatest activity is between the ages 18 and 30. The existence of the active disease at this period will always excite a fear of rapid progress. In children the disease sometimes becomes very chronic, although usually rapid. In elderly people, or, it may be said, over the age of 45, the disease is often only very slowly progressive.

Sex.—Women, on the whole, exhibit less resistance to the disease than men, and are attacked at a rather earlier age. Child-bearing has a very unfavourable influence on the course of the disease.

Heredity.—Cases in which there is a family history of phthisis, on the whole, do worse than those in which there is none, and one may be guided in prognosis by the type which the disease has assumed in other members of the family, especially in brothers or sisters. If the disease has been rapidly progressive, or has run a favourable course in the collaterals, it will probably be so in the patient. J. E. Pollock has instanced a case where nineteen members of a family of twenty-two died at the age of 19.

Constitution and habits.—It goes without saying that if the patient comes of a healthy stock, is of good physique, and has previously exhibited a sound constitution, he is more likely to do well than a man with bad family history, of poor physique, and previously weakly, and a history of bronchitis, pleurisy, or pneumonia. The man who has been intemperate, or has led a life of debauchery, will be less resistant to the progress of the disease than he who has proved himself temperate in all things.

Environment.—The circumstances of the patient have much to do with the prognosis. The possession of affluent means commands many of the elements most advantageous for favourably influencing the progress of the malady, such as good food, hygienic surroundings, and residence in a suitable climate, with possibilities of abundant sunshine and fresh air. Straitened circumstances, on the other hand, put such important remedial agencies out of the patient's reach. This is well shown by the different estimates of the duration of life among the well-to-do and the lower classes. C. T. Williams gives seven years and eight months as the average duration, among 198 cases occurring in private practice followed to a fatal termination. J. E. Pollock gives an average duration of nineteen months for males, and twenty-two months for females, founded on 828 hospital cases.

Rate of progress.—It has been already mentioned how unfavourable is the prognosis in the acute pneumonic type. Great activity and swift pro-

gress, shown by rapidly spreading consolidation, or the quick formation of cavities, or extension of those already formed, are always of grave omen. Slow progress of disease, as shown by the stationary character of the physical signs and their limitation to the part in which they were originally situated, is good.

Extent and stage of disease.—The limitation of the disease to a single lung, and to the upper part of that, is favourable. Evidence of induration and fibrosis is good. Thus flattening of the side and intense wooden dulness, along with good general condition, indicate very chronic non-advancing disease. On the other hand, diffusion of disease through both lungs and the absence of evidence of induration are unfavourable. The cessation of râles and retraction of the chest wall, where previously râles have been abundant, is favourable.

Expectoration.—Profuse expectoration is a bad sign. The diminution of amount is good. When the expectoration consists only of a small amount of tenacious mucus, it is favourable. The presence of elastic fibres in the sputum shows that destruction of lung tissue is still going on.

Bacilli in the sputum.—Great abundance of bacilli, on repeated examination, is a bad sign. The disappearance of the bacilli in a case where they were formerly abundant is very favourable, provided this is accompanied by improvement in the patient. Not much help in prognosis is afforded by a frequent examination of the sputum for bacilli.

Pyrexia.—High and continued fever is always a bad sign. Although normal or nearly normal temperature is generally favourable, and points, as a rule, to quiescence of disease, patients sometimes go steadily down-hill without much rise of temperature.

Bronchitis.—The coexistence of bronchitis with phthisis is unfavourable. It creates a suspicion that the disease has become disseminated throughout the lungs.

Pneumonia is an anxious complication and often proves fatal, but it may be perfectly recovered from.

Hæmoptysis.—Cases in which hæmoptysis occurs early in the disease often run a very favourable course. Cases in which hæmoptysis is frequently repeated do not, as a rule, do well. Hæmoptysis in the later stages is generally unfavourable.

Pneumothorax.—The most favourable statistics give the general mortality of pneumothorax as 70 per cent. The risk to life is greatest during the early period, and as a rule this complication is followed by death in a short time, if it affects, as it frequently does, the less diseased side. When there is little disease on the side opposite to the pneumothorax, the patient may do well. I have known a patient to recover from two attacks of pneumothorax, one on each side, as happened in a case recorded by Samuel West. Magee Finny has recorded a case of recovery after recurrence of pneumothorax on the same side. The cases which do best are those in which no effusion occurs.

Digestive system.—The appetite and digestion form an excellent index as to the general condition of the patient. It is a good sign when the tongue is clean, the appetite good, and powers of digestion unimpaired. A furred tongue, with persistent anorexia and feeble digestion, is a bad sign, unless a better condition of things can be brought about by means of treatment. Diarrhœa occurring in an advanced stage of the disease is usually an ominous sign, especially when it is not amenable to treatment. Peritonitis usually proves rapidly fatal.

Nervous system.—The existence of a condition of morbid erethism and general excitability is unfavourable. Those of a phlegmatic and stable temperament are likely to do better than the flighty and highly strung. The excitable person readily becomes feverish, sleeps badly, and exhibits a restlessness of mind and body which have a bad general effect. The occurrence of insanity or evidence of cerebral tubercle is highly unfavourable.

Prophylaxis.—The prophylaxis of pulmonary tuberculosis is one of the most important questions of the present day. On the one hand, there are some who take an extreme view and regard every case as dangerously infectious, demanding compulsory notification, disinfection, isolation, and periodical inspection. On the other hand, there are men of large experience who, while admitting the possibility of infection, are not of opinion that there is much to be feared from it. I have been careful at the outset to point out that while the disease is always the result of infection, it is not always infectious. Many of the local forms of tuberculosis as well as cases of acute miliary tubercle are, as a rule, non-infectious. In them there is no discharge of bacilli outside the body.

The disease is only infectious when, first, there is some external discharge of tuberculous matter; and, second, this discharge contaminates food or drink, or is allowed to become dry and in the form of dust contaminates the air. One important branch of prophylaxis consists in the disposal of the sputum and the prevention of it from becoming dry or contaminating food or drink.

The tuberculous patient who expectorates, unless he follows simple rules to be presently specified, is a common danger to the community. The tuberculous patient who swallows his expectoration is reinfecting himself, but is for the time being non-infectious to the community. The fæces of a tuberculous patient may be infectious if he is swallowing his expectoration, or if he has ulceration of the intestines, but the chances of their becoming dry or contaminating food or drink are very small.

Much can be done towards the prevention of tuberculosis, by educating the masses as to the proper means of disposing of the expectoration. For the protection of their own families, and to prevent the spread of the disease among the general public, consumptive persons should act on the following simple rules, which have been drawn up by the National Association for the prevention of consumption. " The consumptive person must not expectorate about the house, nor on the floor of any cab, omnibus, tram-car, railway carriage, or other conveyance. Spitting about the streets, or in any public buildings (churches, schools, theatres, railway stations, etc.), is a dangerous as well as a filthy habit. The consumptive person must not expectorate anywhere except into a special vessel or cup kept for the purpose, and containing a little water. When out of doors, a small, wide-mouthed bottle with a well-fitting cork may be used; or a pocket spittoon, which may be obtained from any chemist. For wiping the mouth, a rag or paper, which can afterwards be burnt, should be used instead of a handkerchief. The collected expectoration must be carefully burnt on the back of the fire, at least once daily; this is the simplest, quickest, and safest way of destroying the germ. When there is no fire, the expectoration must be washed into the drain or buried in the earth. The cup or spittoon must then be well washed with boiling water. When not provided with a proper vessel, a consumptive person must not spit into a handkerchief, but into a piece of rag or paper, which must be burnt.

Consumptive persons must not swallow their expectoration, as by so doing the disease may be conveyed to parts of the body not already affected. A consumptive person must not kiss, or be kissed, on the mouth." Notices forbidding spitting should be put up in workrooms, public buildings, railway stations, and conveyances. A tuberculous person should not act as wet nurse, and should not be employed as cook, nurse-maid, or attendant on healthy persons. It is always advisable that a tuberculous subject should sleep alone, and if possible have a separate room. All rooms inhabited by consumptive persons ought to have an especially large amount of sunlight, or at least daylight, and be efficiently ventilated and kept thoroughly clean, being cleansed with wet, not dry, dusters and brooms, so as to avoid accumulation of dust, and to prevent dust flying about in the air of the room.

When a patient becomes confined to bed, the greatest cleanliness is necessary, and every care should be taken to avoid the soiling of the linen with expectoration or fæces. The sheets should be frequently changed, and these and the bedding treated in the same way as in a case of enteric fever. Every room or house in which a consumptive person has lived or died should be thoroughly cleansed, or, still better, disinfected before it is again inhabited.

At the present time there is a lamentable want of provision for advanced cases of phthisis among the working and poorer classes. Hospitals will not take them in. The refuge of the workhouse infirmary is often refused by them. The husband or wife, as the case may be, and perhaps a family of small children, share the sick person's room until death ends the scene. These are the cases which are most likely to propagate the disease. A sufficient number of properly equipped hospitals for cases of advanced phthisis is urgently needed in all large centres of population.

We have stated elsewhere what we believe undoubtedly to be the case, that the principal mode of infection is from man to man, and we consider that it is in this direction that the greatest good can be done. Infection from the lower animals to man is another mode which must be borne in mind. We have pointed out the enormous prevalence of tuberculosis among cattle and the dangers arising from infected milk or meat, and shown how this danger can be removed by boiling the milk and thoroughly cooking the meat.

The prevention of tuberculosis among cattle may be best attained by attention to the hygiene of the cowsheds and by periodical testing by means of tuberculin, and the complete separation of all animals found to be infected from those which are free from tubercle. The calves of tuberculous cows should be separated from their mothers and brought up on the milk of healthy animals. No infected animal should on any account be permitted to remain in a dairy.

As regards the person who is non-tuberculous, he will best escape infection by leading a healthy life, by living soberly and simply, by keeping his muscles in tone by exercise, his blood properly oxygenated by fresh air, and his skin in good condition by baths, and by seeing that his dwelling is clean and well ventilated.

Marriage.—The physician will never sanction marriage in a case where there is evidence of active tuberculous disease. He will often be consulted as to the advisability of marriage in a case where the disease is arrested. The important points are, first, the effect of married life on the patient's

own health; second, the risk of infecting the spouse; and, third, the pre-disposition to tubercle of the children, if any. No doubt the safest rule to lay down is, that no one who shows or has shown signs of pulmonary tuberculosis should marry. This rule is one which patients will not follow, unless it suits them to do so. On the health of the man who is temperate in all things, and is possessed of sufficient means to support a wife in comfort, marriage can have no deteriorating effect. In the case of the woman it is different. The risk of child-bearing is one which has already been referred to. Pregnancy and parturition, especially when repeated, are likely to have an unfavourable effect on the course of pulmonary tuberculosis, and quicken arrested disease into renewed activity. With regard to the second point, if the disease is really arrested, there is, for the time, no risk of infection. Even in the case where there is expectoration containing bacilli, proper precautions as to its disposal should prevent infection; but it is always advisable in such cases that the husband and wife should occupy separate beds. The third question, as to the effect on the issue of the marriage, is a very important one. There is much evidence to show that the children of a tuberculous parent offer less resistance to bacillary infection than the children of non-tuberculous parents. We believe that they require special care and watchfulness, but that with these and a healthy environment they are likely to grow up as strong as other children.

Treatment.—The treatment of pulmonary tuberculosis may be considered under various aspects—medicinal, dietetic, hygienic, and climatic. These again may be discussed as they concern the disease itself or its complications.

We propose first to say a few words concerning some of the medicinal substances which have been found by experience to be serviceable and to have a favourable influence on the course of the disease. We shall then consider treatment as directed to the relief of symptoms and complications. After this, we shall briefly discuss diet, hygiene, and climate, and their uses in the disease. Finally, we shall give a brief summary of the attempts which have been made to treat the disease from the bacteriological standpoint.

Medicinal.—For half a century cod-liver oil has been highly esteemed as a remedial agent. Under its use gain in weight and strength is observed. The researches of Heyerdahl show that the oil is not a simple mixture of olein, palmitin, and stearin, but to the extent of 40 per cent. contains two glycerides of peculiar fatty acids which are very unstable and difficult to isolate. It is probably to the presence of these bodies that the oil owes its effect, and it is useless to attempt to separate something from the oil which could be used as a substitute. In practice, a common mistake is to prescribe the remedy in too large doses. A teaspoonful twice a day is generally sufficient at first, and it is seldom necessary to give more than twice as much later on. The best time of administration is about half an hour after meals or at bedtime. The oil should never be given before food. Patients vary extremely in their ability to take oil. Some can take large doses without the least inconvenience. Others are nauseated by the smallest quantity. On account of the nauseating properties of cod-liver oil, various modes of exhibiting it have been devised. Of these the most palatable and readily tolerated is the mixture with malt extract. From 25 to 35 per cent. of oil is present in the ordinary mixtures. The malt extract has a slight nutritive value, but it is very doubtful whether in this combination

its starch-converting power is of much importance. Emulsions contain about the same proportion of oil, perhaps a little more. Apart from the greater ease with which it is swallowed, there is probably not so much benefit in a tablespoonful of emulsion as in a dessertspoonful of oil. The oil may also be given in capsules, and in some cases inunction may be usefully employed. Preparations known as morrhuol and wine of cod-liver oil, supposed to represent active principles of the oil, are probably of little value. The light-brown oil, which probably contains decomposition products, is more nauseous and less easily tolerated by the stomach than the ordinary oil. Among useful substitutes for cod-liver oil, pancreatic emulsion and petroleum emulsion may be mentioned.

Of late years, creosote has been very extensively employed. It is given in gradually increasing doses. To begin with, 1 minim three times a day is taken, then 2 minims, and so on, until doses of 10 or 15 minims or even more are reached. It has a disagreeable taste, and is most readily taken in capsules containing 1 to 5 minims each. Milk covers its taste fairly well. It should be taken after food. The best evidence of its good effect is the improvement in the appetite which frequently follows its administration. Cough and expectoration are often favourably influenced. It has no specific action, however, on the tuberculous lesions.

Still more recently guaiacol and carbonate of guaiacol have been introduced. Guaiacol, which is one of the principal constituents of creosote, is less disagreeable in taste than the latter, while the carbonate of guaiacol is quite tasteless. Both are, however, much more expensive than creosote. Guaiacol may be given in the same doses as creosote, and the carbonate in doses of from 5 to 15 grs. Although these drugs have been largely used at the Brompton Hospital, it has not been made out that they have any distinct advantages over creosote, except that of palatability.

Guaiacol has also been administered hypodermically, and benefit has been reported in some cases from its use in this way, when it has failed to do good given by the mouth. To begin with, a minim is injected, and if this is well borne, the amount is gradually increased up to 5 or 7 minims. The injections are usually made into the buttock, the needle being inserted deeply at right angles to the surface. The epidermic method is sometimes employed, the cutaneous area corresponding to the pulmonary lesion being painted with 10 to 30 minims of guaiacol. Many other derivatives of creosote have been used. Among these may be mentioned creosote carbonate or creosotal, a viscous liquid, benzoate of guaiacol or benzosol and guaiacetin, both tasteless crystalline powders, eosote or valerianate of creosote, and geosote or valerianate of guaiacol, and piperidine guaiacolate. These may all be given in capsules or cachets in doses of 5 to 30 grs. or minims, under the same conditions as creosote itself.

Garlic, as recommended by Vivian Poore, seems to have much the same effect as creosote. We may give either the syrupus allii (U.S.P.) in doses of 1 to 3 drms., or cloves of garlic chopped up and mixed with beef-tea, or powdered garlic in capsules, in doses of 3 to 10 grs. An almost insuperable objection to garlic is the odour which it imparts to the breath. Oil of cloves, in doses of 5 to 30 minims in capsules three times a day, is the favourite remedy with some physicians. It has also been administered subcutaneously. Ichthyol has hitherto had a very limited use on account of its extremely disagreeable taste and odour, but those who have succeeded in getting patients to take it speak well of the results. The best

mode of administration is in the form of capsules, with a covering such as keratin, which will not dissolve until the intestine is reached. The dose of the remedy is 20 to 60 grs. a day.

Nuclein or nucleinic acid, prepared from yeast, has been employed of late years. A 1 per cent. solution of nucleinic acid is administered hypodermically daily, in doses of from 60 to 80 minims. Some employ a 5 per cent. solution in doses of 50 minims. The remedy has also been given by the mouth, generally in association with injections. Those who have used it most largely speak well of its effects. Arsenic is often highly beneficial when there is anæmia, and 2 to 5 minims of Fowler's solution may be given in combination with other remedies after meals. Hypophosphites of lime and soda are sometimes useful as tonics, in doses of 5 to 10 grs. They have no specific action, and their beneficial effects in the treatment of phthisis have been greatly exaggerated. Other hypophosphites used are those of iron, manganese, potash, quinine, and strychnine. Iron is valuable when chlorosis is combined with phthisis, but in ordinary cases iron is not very well borne, and it should be avoided when there is a tendency to hæmoptysis.

External applications.—Counter-irritation has always been a favourite mode of treatment. Rubefacients, such as lin. camph. ammon. or lin. tereb. acet., are useful when there is bronchial catarrh. A mustard leaf or iodine paint may be applied over the apices in the stage of infiltration. Sometimes a more powerful counter-irritant, the lin. crotonis, is employed, but it has the disadvantage of leaving scars which are often permanent. When there is pleurisy, whether dry or with effusion, relief may often be afforded by strapping, poulticing, or applications of belladonna.

Food.—It is unnecessary to say that the food should be simple, well cooked, and nutritious. Not only is there often almost complete loss of appetite, but most unsuitable articles of diet are consumed. The loss of appetite is associated with dyspepsia, which must be treated on the lines already laid down. The simple tonic will often cure the dyspepsia, and restore the appetite. Bracing air often works wonders in restoring the appetite. Where the quantity of food taken is obviously too little, it must be judiciously supplemented by milk, butter, eggs, etc. It is often easy to secure that the patient takes two or three pints of milk, two or three ounces of butter, and two or three eggs, in addition to the food previously taken. Such unsuitable articles of diet as pickles, ices, nuts, and sweetmeats should be prohibited. Judicious feeding forms a chief part of the treatment at all sanatoria for consumption.

Koumiss, or fermented mare's milk, has been highly esteemed as a food for the tuberculous. This is prepared in the steppes of the Kirghiz, in Southern Russia, where there are establishments for carrying out the cure. The beneficial effects which have been observed are, no doubt, largely aided by the climate. Kefir, or fermented cow's milk, is used in the Caucasus. The so-called koumiss to be obtained in this country is also fermented cow's milk, artificially sweetened. Many dislike the rather acidulous taste of fermented milk, but, for those who will take it, it is an excellent combination of food and stimulant.

Rest and exercise.—When continuous fever is present, absolute rest is essential. When there are markedly remittent temperatures, rest should still be enforced. When the temperature rises only a degree or so in the evening, exercise may be cautiously prescribed. Whenever shortness of breath on exertion is at all a marked symptom, I am very strongly

of opinion that as little strain as possible should be put on the breathing powers. In such cases I regard violent exercise—as tobogganing, climbing, skating—as dangerous and injurious. Whatever walking exercise is taken should be taken on the flat. The patient should always use the lift to go upstairs, if one is available.

If with moderate exertion there is no shortness of breath, then not only can it do no harm, but the patient will be better for it. The kind and amount of exercise may be determined by the effect on the patient's temperature. If there is a rise amounting to more than one or two degrees after exercise, the amount must be reduced.

Great importance has been attached by Brehmer and his followers to graduated hill climbing, on account of its strengthening effect on the heart. The walks should be so arranged that the patient starts with a short ascent, then has a walk along the flat, and returns home down hill. Walking is the safest form of exercise until the disease has become quiescent. Exercises which bring into action the muscles of respiration are very useful. The following four simple exercises, which have been recommended by Knopf, are given as illustrations. In the first exercise the patient stands erect, with feet together and hands by the side. The arms are then slowly raised from the sides until they are horizontal, the patient slowly inspiring. After a brief interval, during which the breath is held, the arms are lowered more rapidly during expiration. The second exercise is a modification of the first, the movement of the arms being continued until the hands meet over the head. In the third exercise the arms are held out in front, palms outwards, and slowly brought backwards during inspiration until they meet behind the back. The movement is reversed during expiration, each respiratory act being followed immediately by a secondary forced expiratory effort. In the fourth exercise the patient stands straight, places his hands on his hips, with thumbs in front, and then bends slowly backward as far as he can during inspiration. He holds his breath, and returns to original position during expiration.

Clothing, etc.—Among the lower classes, through fear of catching cold, the clothing is often excessive. Two or three thick woollen vests are worn, and the undervest is probably not changed at night. Woollen underclothing should be worn all the year round—thin in the summer, and thick in the winter. The clothing should be sufficient to keep the patient warm, but not too heavy to interfere with exercise. The bedding should be carefully adjusted to the patient's requirements. A thin woollen night-dress is indicated if there are night sweats. The bedroom should be airy, well ventilated, and scrupulously clean. There should be no hangings or curtains which are not washable.

Climate and fresh air.—Of all influences which can be brought to bear on pulmonary tuberculosis, none can be compared with the effects of climate and fresh air. A great deal may be done by altering the mode of life, by securing that the patient occupies well-ventilated, airy rooms, and that, as far as practicable, he should lead an out-of-door life. It is most important to teach the patient to have the windows of the rooms in which he lives widely open, so that the air may always be fresh. Wind, rain, snow, fog, want of sunshine, and sudden changes of temperature are the great trials of the English winter climate. These make it impossible for the phthisical patient to get out of doors on many days of the winter months, and are the fruitful cause of bronchial catarrhs which seriously impede the recuperative process. In the ideal climate

there should be stillness of the air, freedom from fog, moisture, and dust, and abundant sunshine. For those who cannot leave England, it may be consoling to know that good results have followed wintering at Torquay, Falmouth, Bournemouth, Hastings, Ventnor, Deeside, Forres, etc. Their climates are not ideal, but they get a fair amount of sunshine, and they are provided with comfortable hotels. It is possible at most of these places for patients to find shelter out of doors from wind and rain. Two of the best winter resorts in Europe with which I am acquainted are Davos and St. Moritz in Switzerland. The advantages of these resorts are stillness and dryness of the air, freedom from dust, and a considerable amount of bright sunshine. In consequence of the clearness of the atmosphere, the sun's rays have great warming power. As a result of the stillness and dryness of the air, a high degree of cold can be tolerated without discomfort. The air has a wonderfully stimulating effect upon the appetite, and the patient becomes capable of assimilating a much larger quantity of food than is the case at home. Patients are able to spend the greater part of the day in the open air. It is only during the winter, however, that the climate of Davos, or of the Engadine, has special advantages. In May and June the weather is notoriously uncertain, and rain and wind are often prevalent.

It is important to impress on patients who are sent to winter in these parts that health must be put before pleasure. Many who might have benefited from the climate have done themselves harm by over-exertion in skating, tobogganing, the sport of the "ski," dancing, etc. The patient who is anxious to regain his health should spend as little time as possible in the public rooms, should avoid all entertainments, and should be guided as to the amount and kind of exercise by the medical adviser on the spot.

The question arises, whether the rarefaction of the air plays any important rôle in the results of residence at high altitudes. To us it seems impossible to separate this element from the other features, and we do not think that rarefied air *per se* has any appreciable influence, beneficial or otherwise. There are several classes of cases which are unsuitable for the cold high altitude treatment. Such are advanced cases of all kinds, acute cases with high fever, cases in which there is laryngeal disease, heart disease, or albuminuria, cases in which diarrhœa is a prominent symptom, cases in which there is a natural repugnance to cold, and cases of patients of advanced age with emphysema. Early cases in which the disease is not active are those in which the best results may be hoped for.

The Riviera as a resort for tuberculous patients combines considerable advantages with serious drawbacks. It offers bright sunshine and a luminous atmosphere. The air is balmy, genial, dry, exhilarating, and bracing. The scenery is beautiful, the vegetation luxuriant. The drawbacks are, that the winds are chilly and change twice a day, that the mornings and evenings are cold, and that frequently it is too hot in the sun and too cold in the shade. Hyères, Cimiez, Mentone, and San Remo are the most suitable. Nice can never be recommended for cases of phthisis. At Cannes the variations of temperature are great, and special care is required if the invalid is permitted to winter there.

Madeira and the Canaries have always had a considerable reputation as health resorts for consumptives, perhaps greater at one time than they have now. The excessive moisture and relaxing climate of Madeira

render it unsuitable in most cases. Grand Canary is preferable to Teneriffe, and both are drier and more bracing than Madeira.

Farther afield, as a resort for phthisical patients, we may mention Egypt. In winter the desert air is dry, stimulating, and exhilarating. There is, as a rule, an almost complete absence of rain and abundant bright sunshine. The mean winter temperature is 62° F. The disadvantages are like those of the Riviera—occasional cold high winds often accompanied by dust, sudden changes of temperature between day and night, and great differences between the sun and shade temperatures. Cairo is totally unsuited for the invalid, who should winter either at Helouan or Mena House near Cairo, or at Luxor or Assouan up the Nile. Invalids are not advised to remain in Egypt after the end of March or middle of April. Egypt should be avoided by patients in whom there is a tendency to diarrhœa, fever, or active pulmonary disease.

The medical man is often asked his opinion as to the Cape and Australia. It might be as pertinent to ask him his opinion of Europe as a health resort. In many parts of Australia and of the Cape the patient with phthisis is infinitely worse off than in England. In certain parts of the Cape the climate is magnificent, but the sanitary arrangements are generally defective, and the hotels inferior. Graham's Town (1800') in the Eastern Province, Aliwal North (4348'), Cradock (2850'), Tarkastad (4280') with good hotel, and Burghersdorp (4650') in the Karroo, and Bloemfontein (4500') in the Orange River Colony, are among the resorts most favourably spoken of. Recently a large sanatorium has been opened at Kimberley (4360') in Griqualand West.

The large towns in Australia (Melbourne, Sydney, etc.) should be given a wide berth by the tuberculous. Hobart Town in Tasmania, Hay, Deniliquin, and Bathurst in New South Wales, and Toowoomba and Warwick on the Darling Downs in Queensland, are among the most suitable resorts, but in most of these places indifferent food and accommodation must be set against climatic advantages.

In the United States, Colorado Springs (6000'), with a climate in winter much resembling that of Davos in Switzerland, cold but dry and sunny, has a decidedly curative effect. It is occasionally visited by blizzards, but this is almost its only drawback. The Adirondacks and the district about Liberty in Sullivan County (N.Y.) have also a high reputation among American physicians.

A sea-voyage may be suitable in certain cases. Where the disease is early, fever little or absent, and the patient a good sailor, and in easy enough circumstances to travel comfortably, great good may result from a journey to Australia and back by the Cape. Some, even of my poorer patients, who have gone a voyage against my advice, have greatly benefited, although in others the malady has rapidly advanced. Walshe speaks of benefit even in advanced cases, but a voyage can never be advised to such patients. I should feel much more disposed to recommend a sea-voyage after all activity of the disease had ceased, and when it is important to establish the health on a firm basis.

Sanatorium treatment.—It is only during the last few years that the great value of sanatorium treatment has been properly appreciated in this country, although for many years it has been adopted on the Continent. The pioneer in this line of treatment seems to have been George Bodington of Sutton Coldfield, who in 1839 started a home for consumptives, believing that great advantages were to be derived from "systematic

arrangements with regard to exercise, diet, and general treatment, with the watchfulness daily, nay almost hourly, over a patient of a medical superintendent." He advocated a generous diet, and fresh air night and day. Another physician who early insisted on the value of fresh air night and day was Henry MacCormac of Belfast. But it was Hermann Brehmer who first successfully inaugurated the sanatorium treatment in 1859. Firmly believing in the curability of phthisis in its early stages, he started a small sanatorium in Görbersdorf in Silesia. He chose a spot charmingly situated among the hills, at an elevation of 1840'. At this height he fancied that there was a natural immunity from tubercle, and he considered that hill climbing formed an important part of the treatment. From this small beginning the Görbersdorf sanatorium has now become the largest of the kind in the world.

Of the many other sanatoria which have been instituted on lines similar to Brehmer's establishment, the following may be mentioned. Falkenstein (1300'), in the Taunus mountains, conducted for many years by Dettweiler; Reiboldsgrün (2460'), in Saxony, among the Erzgebirge, delightfully situated amidst a dense pine forest; Nordrach Colonie (1500'), in the Black Forest; Hohenhonnef (735'), on the Siebengebirge; Leysin (4750'), in Canton de Vaud, Switzerland, principally frequented by the French; and Arosa (6150'), not far from Davos. We may also add to the list the Adirondack Cottage Sanatorium for poor patients, started by Trudeau, and the Loomis Sanatorium (2200') in Sullivan County, for persons of limited means, both in the State of New York. Recently a large number of private sanatoria for paying patients have been opened in various parts of the United Kingdom. In most of these the arrangements have been modelled on those at Nordrach.

The arrangements at some Continental sanatoria are far from perfect, especially with regard to ventilation of sleeping and public rooms, baths, medical supervision, etc., but on the whole sanatoria are usually a great deal better for patients than the ordinary hotels. Many of the hotels in the high altitudes in Switzerland, as has been said with some justice, seem to have *une spécialité de la viande dure,* and it is a hard struggle for the invalid to eat the ordinary meals of the *table d'hôte.*

The excellent results obtained at such sanatoria as those mentioned show that much may be done in the treatment of phthisis by modifying the mode of life under constant medical supervision, even where the climate is by no means ideal, and the altitude is moderate. The sanatoria usually occupy sites sheltered from the prevailing winds and where surrounding pine woods secure freedom from dust. The mode of treatment adopted at these establishments has for its special features constant medical supervision, the open-air life which the patients are made to lead, the administration of abundant and nourishing food, and the removal from home surroundings, home worries, and the solicitude of over-anxious friends, rest during the febrile stage, and graduated exercises and hill climbing when the fever is past.

To enable the patients to be as much in the open air as possible, there are at some of the sanatoria verandahs and summer-houses fitted with couches where they can recline. The shelters are either open on one side and revolving, or fitted with movable shutters so as to obtain shelter from wind or sun. The patients are led to look for warmth to extra clothing, rather than to shutting out fresh air because it is cold. Weak and elderly patients lie near the open windows in their rooms. In this way the

patient lives more or less continuously in the open air. Exercise is regulated according to the strength of the patients.

The mode of feeding is adapted to individual cases. The food is well cooked, appetising, and varied. Ordinary meals are supplemented by milk, soups, and broths. At Nordrach only three meals a day are allowed, no food being taken between. The quantity of food ordered is sometimes greatly in excess of what is taken by a strong, healthy working man. It must be remembered that the cases which are likely to do well at these sanatoria are the early or inactive cases, and advanced or actively progressive cases should never be sent to them.

Special treatment.—We shall now consider the treatment of some of the special symptoms.

Alimentary system.—It is always important to improve the appetite and strengthen the digestive powers. An alkali in a bitter infusion, taken a short time before meals, sometimes works wonders. A mixture containing 15 grs. of bicarbonate of soda, and 3 minims of dilute hydrocyanic acid to the ounce of compound infusion of gentian, has a great reputation among the patients at the Brompton Hospital. Sometimes an acid mixture containing dilute phosphoric acid with a bitter infusion suits better than an alkaline. If there is constipation it must be relieved. A useful pill in ordinary cases is aloin, 1 gr.; extr. bellad., extr. nuc. vom., āā ¼ gr. One or two of these may be taken in the evening. If the tongue is furred, an occasional dose of calomel will benefit. The treatment of diarrhœa is considered under the heading of Tuberculosis of the Intestines.

Cough.—Routine treatment, whether by sedatives or expectorants, is bad. As far as possible, cough mixtures, linctuses, etc., should be avoided. Relief may be obtained by sipping lemon or barley-water, or toast and water, or demulcent drinks, such as decoction of iceland moss or linseed tea. Lozenges of various kinds are useful, such as troch. ipecac. (B.P.), or troch. glycyrrhiz. (Brompton Hosp. Phar.). If the cough is harassing at night, preventing sleep and rest, a linctus may be necessary. In a linctus, a small dose of dilute sulphuric acid, opium, morphine, codeine, paregoric, or squill, is combined with syrups of various kinds (treacle, honey, or oxymel) and water, care being taken that the preparation is neither too sweet nor too thick. Sometimes inhalations of menthol, creosote, or terebene are more efficient in quieting paroxysms of coughing than remedies by the mouth. Twenty minims of a solution consisting of equal parts of a 20 per cent. alcoholic solution of menthol, creosote, and spirit of chloroform dropped on the sponge of an inhaling respirator, may be mentioned as a useful form of dry inhalation. The ordinary compound benzoin inhalation (tr. benzoin. co., 1 drm. to a pint of water at 140° F.) is sometimes soothing. Sprays to the back of the pharynx may be tried when other measures fail. A 2 per cent. solution·of cocaine or of menthol is very suitable for this purpose. When the cough is accompanied by tickling, smarting, or pricking sensations in the throat, a small blister or mustard leaf, or even a hot poultice, applied externally at the side of the larynx, will sometimes relieve.

Fits of coughing, terminating in vomiting, sometimes come on just after a meal. In such cases the soda mixture previously mentioned may be of service. Sometimes 5 minims of liquor potassæ, with 5 grs. of alum, taken shortly before the meal, will prevent the cough and vomiting. In other cases, a dose of a few drops of laudanum, chlorodyne, or tincture of nux vomica before the meal proves more efficacious.

Hæmoptysis.—The patient should be kept in bed at perfect rest until the bleeding has entirely ceased. He should not be allowed to talk. In the case of a first hæmoptysis, and sometimes in subsequent attacks, the patient is in a highly nervous state, and the physician can do much to allay his fears. A hypodermic injection of morphine ($\frac{1}{4}$ gr.) will soothe the patient and produce that condition of repose which is so essential. An ice-bag may be applied to the front of the chest if the hæmorrhage continues. A hot-water bottle to the feet is advisable, if they are at all chilly.

The diet should be limited to two pints of milk, with a little bread and butter, custard, or jelly, as long as the hæmorrhage continues. Stimulants, it is needless to say, should be forbidden. Various hæmostatics have been used from time to time. Hamamelis, oil of turpentine, and ergot are the best of these. Twenty to 60 minims of the tincture of hamamelis, 10 minims of oil of turpentine in capsules, or 1 to 3 grs. of ergotin in hypodermic injection, may be given.

When hæmoptysis is persistent, either stimulants or depressants may be required. If the pulse is rapid and feeble, digitalis and alcohol, cautiously administered in small doses, may do much good. In such cases the bleeding is probably kept up by passive congestion. If, on the other hand, the pulse is strong and sustained, antimony sometimes acts better than any other remedy. A solution of tartar emetic, 1 gr. to the half-pint, may be ordered, and the patient may take of this a teaspoonful every half-hour, while the effect is watched. Attention should be directed to the state of the bowels. A mild purge is advisable in ordinary cases. When the patient is plethoric or alcoholic, aperients form the most important part of the treatment. A couple of grains of calomel may be given at night, followed by a saline aperient mixture in the morning, and repeated when necessary.

Sweating at night is often a source of great discomfort to the patient, and its treatment necessarily demands attention. The amount of clothing and the proper ventilation and temperature of the sleeping apartment must be studied. It is well, when the sweating occurs in the early morning, that the patient should be sponged with tepid water, and should have a small amount of food and stimulant at that time. The whole of the body should be frequently washed with warm water.

There are several remedies which exert some control over night sweating. Among these are oxide of zinc, belladonna or atropine, nux vomica or strychnine, agaricin, picrotoxin, and camphoric acid. Five grs. of oxide of zinc may be given in the form of a pill, alone or combined with half a grain of extract of belladonna. Liquor atropinæ sulph. may be given in minim doses, extract of nux vomica in half-grain doses, liquor strychninæ hydrochloridi in.10 minim doses, agaricin in doses of $\frac{1}{12}$ gr., picrotoxin in doses of $\frac{1}{60}$ gr., and camphoric acid in doses of 20 to.30 grs. Sometimes one remedy will succeed when another fails.

The medicinal treatment of fever has not, so far, been very successful. Every known antipyretic has been tried more or less, but with very little apparent result on the temperature, and but little benefit to the patient. As a rule, the case should be treated on general principles.

Whenever there is continued fever, the patient should be kept at rest in bed; but when fever is only slight, the morning temperatures normal, and but little elevation at night, he may be up most of the day. Persistent fever, although an indication for rest in bed, does not contra-indicate sunshine

and fresh air, and, whenever possible without disturbance or fatigue, the patient should be allowed out of doors.

Tepid sponging, at the time when the temperature is highest, will often promote the comfort of the patient. Cradling is another method for reducing the temperature. In this method the bedclothes are raised from immediate contact by means of a wire bed-cradle, the cooling effect of which may be increased by the suspension of ice-bags underneath the cradle. If the latter are used, care should be taken to prevent dripping from the condensed vapour which collects on their exterior.

Pneumothorax.—At the outset, if there is shock, diffusible stimulants should be given, and if pain and nervous excitement, opium or morphine should be administered. If there is much dyspnœa, relief may be afforded by tapping by means of a syphon arrangement. If, in spite of this, dyspnœa increases, dry or wet cupping or venesection are sometimes useful. In the later stage, if fluid is effused, part of it should be drawn off by syphonage after a few weeks. In the case of a pyopneumothorax, opinions are divided as to the best mode of treatment. Many surgeons are opposed to operative measures. Samuel West, however, strongly advocates treatment by incision and drainage, as in the case of empyema. Tapping never affords more than temporary relief in pyopneumothorax.

Treatment of chronic tuberculosis from a bacteriological standpoint.—Two kinds of immunity are now recognised in the diseases due to bacteria. One is immunity to the toxine produced by the bacilli, the other is immunity to the bacilli themselves. Thus, animals can be immunised against the toxine of tetanus but not against the microbes; while, in the case of enteric fever and cholera, they can be immunised against the microbes but not against the toxines. To be complete, immunity should combine both these elements. The ordinary course of pulmonary tuberculosis does not encourage the hope that any natural immunity is produced. The malady may go on for years without any sign of immunity appearing. Fresh outbreaks, as we know, are not uncommon even after arrest has occurred.

Certain facts observed by Koch encourage the belief that immunity is possible. In acute miliary tuberculosis there is a stage in which the bacilli, at one time abundant, become so few that they are difficult to find; and this disappearance is the more remarkable, because ordinarily the bacilli, even when dead, are absorbed very slowly indeed. This suggests that a process of immunisation, purely bacterial, has been brought about, but too late to be of benefit. Koch believes that in these cases of apparent immunisation the body is as it were inundated in a short time with the micro-organisms. The immunity only comes after absorption or digestion of the bacilli. The reason that no immunity ordinarily occurs, is that the bacilli attain their development only in small numbers in the human body. They are environed by dead tissues, and are only absorbed long after when they are themselves dead, and have undergone profound changes. In the parts where the tubercles grow, as in cavities and at the surface of mucous membranes, the bacilli are eliminated without undergoing modifications, and are not absorbed at all. The problem to which Koch set himself was to try and bring about artificially this absorption and digestion of the bacilli. Koch first attempted to extract from the bacilli their active principle, and by administering subcutaneous injections of the extract to bring about immunity. In this, as we shall see, he was not altogether successful.

Recently, by pulverising the bacilli, he has obtained principles incapable of extraction otherwise.

Tuberculin, a principle extracted from the bacilli, was originally introduced by Koch (1890) as a curative agent. The mode of preparation was as follows. The bacilli are grown for six or eight weeks in a slightly alkaline veal broth, to which had been added 1 per cent. of peptone and 4 to 5 per cent. of glycerin. The medium containing the bacilli, having been evaporated to a tenth of its bulk in a water-bath placed in boiling water, is filtered through porcelain. The filtrate is tuberculin, a clear brownish fluid containing 40 to 50 per cent. of glycerin, which keeps it aseptic. If any bacilli are present in the liquid, one may rest assured that they have been killed by the mode of preparation.

Various attempts have been made to purify the tuberculin so prepared. On treatment with alcohol a precipitate is obtained. This precipitate, dissolved in water and treated with a mixture of alcohol, chloroform, and crystallised benzol, is the tuberculocidin of Klebs. To a liquid still further purified, Klebs has given the name of antiphthisin. Tuberculin in doses of 0·25 c.c. produces an intense reaction in a healthy adult. In a tuberculous adult a much smaller dose, 0·01 c.c., produces both a general and a local reaction. Four or five hours after the injection the temperature rises 4 or 5°, and this rise is often ushered in with a rigor and attended by general malaise, pains in the limbs, and sometimes vomiting. These symptoms pass off in twelve to fifteen hours. The local reaction can be best studied in cases of cutaneous tuberculosis. The lupus patch reddens and swells up, even before the constitutional symptoms manifest themselves. The swelling diminishes in general with the fever, and the patch becomes covered with crusts formed by dried exudation, which separate at the end of two or three weeks. A similar but slighter local reaction can be observed in the case of tuberculous glands and joints. In the case of pulmonary tuberculosis, there is an increase of cough and of expectoration, together with signs of increased activity of the local disease. By repetition of the dose, it is possible to greatly increase the amount which can be borne.

In the subject of pulmonary tuberculosis a much smaller dose is needed to produce reaction than in the case of lupus. Thus, 0·001 c.c. may at first be sufficient to produce a marked reaction, although later 0·01 c.c. or more may be borne with even less reaction. Although Koch had great hopes that tuberculin was curative, and believed that the tolerance of the substance gradually brought about was due to the progressive destruction of the tuberculous tissue, these hopes were not realised. Even in the case of lupus, the improvement was found to be only temporary. The reaction following the administration of tuberculin proved to have a high diagnostic value, and much use has been made of it for the recognition of tuberculosis in cattle. Opinions differ, however, as to its worth as a diagnostic agent in early tuberculosis in the human being. It is known that the reaction occurs in cases of leprosy, syphilis, actinomycosis, and cancer.

For diagnosis the initial dose should be 0·005 c.c. If this gives no reaction, another dose of 0·01 c.c. may be given in three days' time. If this has no effect, a third of 0·02 c.c. may be administered. If slight symptoms are produced by a dose of 0·02 c.c., a fourth injection of 0·03 c.c. may be necessary to attain a positive conclusion.

A new tuberculin was more recently (April 1897) introduced by Koch. Dried cultures of tubercle bacilli are ground up in an agate mortar. The resulting powder is mixed with distilled water and centrifugalised. The solid

residue so obtained is dried, again pounded, mixed with distilled water, and the liquid centrifugalised. The process can be repeated until no residue is left. The liquid obtained from the first centrifugalisation is called tuber-culin-O (*oberste*). That from the second and subsequent centrifugalisations is called tuberculin-R (*rest*). The tuberculin-O produces almost identical results with those of ordinary tuberculin, while tuberculin-R does not pro-duce reaction except in large doses, but, according to Koch, possesses immunising properties. Tuberculin-R has not realised expectations either as an immunising or therapeutic agent.

Maragliano and others have attempted to produce an immunising or curative serum. Animals are inoculated in gradually increasing doses, with toxic substances derived from virulent cultures. The animal is, after a time, found to resist the injection of cultures virulent enough to kill a control animal. Treatment with serum of an animal so immunised must be considered to be at present still in the experimental stage.

TUBERCULOSIS OF THE GENITO-URINARY SYSTEM.

URINARY ORGANS.

Etiology.—Tuberculous disease of the kidney is usually primary, although some have held that it is often secondary, arising by extension upwards along the ureter from tubercle of bladder or genital tract. Some have even maintained that the cause was direct infection of the generative organs, as, for example, from a tuberculous husband to a healthy wife. Such a mode of infection is out of the question in a large proportion of the cases met with in practice.

At first the disease is limited to one kidney; and, when both are attacked, it is always more advanced in one than in the other. Fagge found, out of thirty-four cases, in twenty-two one kidney only was involved. The left kidney has been observed to be rather more frequently the seat of tubercle than the right. Out of eight fatal cases at St. Thomas's Hospital, in four both kidneys were affected, and one only in the remainder. Tuber-culous disease of the bladder is more often secondary than primary, but cases of the latter type do occur. It is more common in males than in females, and most frequently occurs in the age period twenty to thirty.

Morbid anatomy.—Miliary tubercle commonly occurs in the kidney, when there is general miliary tuberculosis. It was noted present in thirty-four out of 496 cases of pulmonary tuberculosis, examined post-mortem at the Brompton Hospital. The tubercles appear as greyish white spots, about the size of pins' heads, and are generally most easily recognised on the sur-face after stripping off the capsule, although they may also be seen scattered through the organ. They are usually comparatively few in number.

Caseous tubercle in the kidneys may be met with in the form of scattered nodules in cases of pulmonary tuberculosis, but most frequently it is found in the form of local tuberculous disease of kidney, scrofulous kidney, or renal phthisis, as it has been called. This form is very rarely secondary to pulmonary tuberculosis. Caseous tubercle is most frequently deposited at the apices of the pyramids, but may be found anywhere, either in the cortex or medulla. Sooner or later the caseous mass softens, and is discharged, either directly into the pelvis, or is retained in the interior of an abscess cavity. The kidney substance is gradually destroyed, and cavities are formed, with caseous walls separated by septa.

In advanced cases the organ may be converted into a multiloculated cyst, with little or no kidney substance remaining. A perinephritic abscess sometimes forms about the diseased organ. The organ, as a rule, is but little enlarged, except when there is obstruction of the ureter and pyonephrosis. The pelvis of the kidney, sooner or later, is affected, and its interior becomes lined with cheesy material. Its cavity probably dilates, and is filled with curdy pus, and occasionally calculi form in its interior. The ureter, also, in many cases becomes diseased. Its mucous membrane may be studded with tubercle, or ulcerated in patches or throughout its entire length, while on its interior curdy matter is deposited. The walls may be extremely thickened, while the lumen is narrowed, and occasionally may be completely occluded. Very rarely the ureter may be the only part of the urinary tract affected.

The mucous membrane of the bladder, like the kidney, may be invaded by miliary tubercles, which may be few or numerous. Nodules of crude caseous tubercle, and ulcers, varying in size, shape, and depth, may also be present. At first the ulcers are quite superficial and small, but they tend to spread and coalesce, and increase in depth. The most usual situation is about the apex of the trigone, but no part of the mucous membrane may escape. Cases have been reported where the entire mucous membrane has been destroyed by ulceration, and the muscular coat covered by a deposit of caseous yellow matter. The capacity of the bladder is greatly diminished, and the walls are thickened partly from muscular hypertrophy and partly from chronic inflammation. Sometimes the ulcerated surface is the seat of a deposit of lime salts. Very rarely the ulceration has caused perforation of the bladder and acute peritonitis. Tuberculous ulceration may extend into the urethra for an inch or so. Very rarely tubercles or ulcers may be found in its entire length, up to an inch or so from the meatus. In fatal cases it is quite exceptional for the kidneys to be tuberculous, and the bladder to escape; but sometimes the bladder is affected without the kidneys, and *vice versâ*. Tuberculous deposits are nearly always found to be present in other organs.

Symptoms.—Miliary tubercle in the kidneys or bladder produces no symptoms by which its presence can be recognised. The symptoms caused by the other forms of tuberculous disease of kidney are not in themselves specially characteristic. There is usually pain in the corresponding loin. The affected kidney can sometimes be felt to be distinctly enlarged, and may be tender to manipulation. Often the organ is little, if at all, increased in size.

The urine sometimes is quite normal. It is generally acid, and often contains pus, and sometimes albumin. The patient may have observed that it is thick and muddy, or that it deposits a sediment on standing. Hæmaturia is not at all uncommon. It was noted in eight out of twenty-three cases treated at St. Thomas's Hospital; and Fagge found that it was recorded in ten out of eighteen fatal cases at Guy's Hospital. The quantity of blood is not usually large, although exceptionally the bleeding has been prolonged and profuse. By far the most important sign is the presence of the tubercle bacilli in the urine. The discovery of these is greatly facilitated by centrifugalising, for the bacilli are generally few in number, and may easily be missed. It may be well, in some cases, to try the effect of inoculating guinea-pigs with the sediment. This is said to have given positive results in some cases where tubercle bacilli have not been found.

It is very important not to mistake the smegma bacillus for the

tubercle bacillus. The smegma bacillus may be detected in the urine in a large proportion of female cases, although it is rarely present in male cases. All urine which is to be examined for tubercle bacilli should, in the case of females, be drawn off by catheter. Grethe says that by counter-staining with concentrated alcoholic methylene-blue, after staining in the ordinary way with carbol-fuchsin, the tubercle bacillus is easily identified by its red colour, contrasting with the blue of the rest of the preparation, including the smegma bacillus. Grünbaum states that the smegma bacillus can be readily differentiated from the tubercle, by the fact that two minutes' immersion in dilute alcohol will decolorise the former, but not the latter.

Frequently, superadded to the symptoms already mentioned, we get others connected more immediately with the bladder. Thus there may be suprapubic pain. Most commonly there is abnormal irritability of the bladder; the patient has to pass water at short intervals, and there is pain or discomfort in micturition.

Diagnosis.—In the absence of evidence of tuberculous disease elsewhere in the body, a positive diagnosis may be impossible until the discovery of bacilli in the urine. The disease may be confounded with renal calculus. Sometimes calculus is present along with tuberculosis. In renal calculus the pain is, as a rule, more decided, and hæmaturia is more frequent, while the urine likely does not contain pus.

Hydronephrosis may sometimes be mistaken for tuberculous disease. In this case there is a more distinct tumour, which is often lobulated. More diagnostic is the variation in size of the tumour, which sometimes actually disappears, this being immediately preceded by the passage of a large quantity of urine. Sometimes the ureter has been so thickened by tuberculous deposit, that it could be felt through the abdominal wall as a hard, rigid cord.

Prognosis.—The prognosis cannot but be gloomy as regards recovery. Still the duration of the disease is sometimes long. Thus, in five cases out of twenty-three observed at St. Thomas's Hospital, the disease had lasted over four years, the average duration being six years. In the remainder the duration was shorter—from six months to two years. Where one has reason to believe that the disease is primary in the kidney, and that it has not spread to the bladder or to the other kidney, the possibility of radical cure by nephrectomy must be borne in mind.

Treatment.—A case of renal or vesical tuberculosis may be treated on general principles, such remedies being employed as are found to benefit in tuberculous disease elsewhere, but little prospect of arrest or cure in this way can be held out. Unfortunately, the patient does not as a rule apply for relief until the disease has made considerable progress. There can be no question that when tuberculosis is limited to one kidney, that kidney should be excised. We know that if such a case is left to itself, the disease will gradually extend in the kidney, will probably spread along the pelvis to the ureter and bladder, and that sooner or later the other kidney will be affected. The difficulty we are in, is in determining how far the disease extends in a particular case.

If the bladder is already involved, I do not consider anything is to be gained by surgical treatment of the renal disease. If it is not, and the renal symptoms are of comparatively short duration, I should be disposed to recommend an exploratory operation. The results of operative treatment for tuberculous kidney, so far reported by surgeons, are not very encouraging, probably because operation has been put off till too late. A

mortality of 27 to 40 per cent. has been recorded from nephrectomy, and an even higher rate from nephrotomy.

In tuberculosis of the bladder, tonic and hygienic treatment gives the best results. Remedies such as hyoscyamus, liquor potassæ, and citrate of potash are useful in relieving irritability and frequency of micturition. I have seen no benefit, but rather the reverse, from iodoform injections, the use of which has been advocated by some surgeons. Even washing out the bladder with warm boracic lotion (3 to 4 per cent.) sometimes seems to do more harm than good. Surgical treatment is only called for when there is persistent irritability and tenesmus. To relieve these troublesome symptoms, suprapubic cystotomy has been performed, and drainage has been established for several months. The rest given to the part in this way acts as the curative agent, and great relief has sometimes been afforded. Scraping of the ulcers, or other active treatment, is difficult to carry out efficiently. Attempts have been made to increase the capacity of the bladder by gradual distension with fluid.

TESTICLE.

Tuberculous disease of the testicle, like that of the kidney, is frequently primary, although often complicated with tubercle in other organs. As a rule, one organ only is affected. Tubercle, as a rule, first attacks the head of the epididymis, although some authorities hold that the disease most frequently begins in the globus minor or tail. The disease, however, wherever it may begin, soon involves the whole epididymis in the form of caseous nodules, which may soften and finally discharge externally, the scrotum previously becoming adherent. The disease after a time spreads into the testicle, tubercles appearing first in the corpus Highmorianum. Caseous nodules may also be found in the body of the testicle. The vas deferens and the vesiculæ seminales may be secondarily involved, and lined with caseous material. As the result of this, the vas may be felt to be thickened. The prostate also is likely to be the seat of caseous deposit, being similarly affected, consequent on tubercle of bladder or kidney. Sometimes a tuberculous abscess forms in it. Tuberculous testis may occur at any age. Of forty-six cases treated at St. Thomas's Hospital, the age distribution was as follows :—

− 5	− 10	− 20	− 30	− 40	− 50
8	5	4	13	9	7

Symptoms.—There may be no symptoms apart from the enlargement of the organ and the inconvenience of a sinus. Probably pain only occurs when an abscess is forming.

Diagnosis and prognosis.—The diagnosis has to be made from syphilitic disease and new growth. Syphilis attacks the body of the testis, producing a painless, smooth, hard, heavy, uniform swelling, which seldom breaks down. The cord, as a rule, is not thickened. With syphilis, hydrocele is frequently present; with tubercle, it is uncommon. New growth usually produces a solid, smooth, firm enlargement of the testicle, and there is little tendency to ulcerate through the skin. The lumbar, and sometimes the inguinal glands, are secondarily affected. In some cases the disease becomes arrested, the caseous tubercle becoming encapsuled or discharged. There is, however, a strong probability that secondary trouble will arise.

Treatment.—This is principally a question for the surgeon. Castration or epididymectomy certainly appears to be indicated where the disease is localised. Scraping may be an adequate means of removing the diseased tissue in some cases.

FEMALE GENERATIVE ORGANS.

Tuberculosis of the female generative organs may occur at any age. It is usually secondary to tuberculosis elsewhere, but may be primary, and be followed by pulmonary or generalised tuberculosis. In the secondary cases the virus is conveyed by the blood, or spreads by continuity from neighbouring organs. The primary cases may result from direct infection. It is difficult to obtain direct evidence of this in man. That tuberculosis of the female genitals may be so produced is shown by certain experiments on animals. The introduction of cultures of bacilli into the vagina of guinea-pigs has been followed by the production of sub-epithelial tubercles in the uterus. Moreover, guinea-pigs and rabbits impregnated by males, into whose testicles the tuberculous virus had been previously introduced, became tuberculous themselves, with pronounced lesions of the vagina and uterus.

While every portion of the genital tract may be affected, the most common seat of the disease is the tubes. Next in order of frequency comes the uterus, then the ovaries, vagina, cervix, and vulva. Both tubes are generally involved, although sometimes the disease is limited to one.

The tubes become greatly enlarged, and sink behind the uterus, forming large sausage-shaped tumours. They are usually adherent to the surrounding structures, and the fimbriated extremities become occluded. The lumen of an affected tube is dilated, and the interior is filled with yellow caseous material, which may be of pus-like consistence, or hard and solid from calcification. It is often impossible to distinguish such tubes with the naked eye from those of ordinary pyosalpinx. Sometimes a tubal abscess ruptures into the bowel. Infection of the tubes often takes place from the peritoneum. They are found to be tuberculous in from 30 to 50 per cent. of all cases of tuberculous peritonitis in women.

In the uterus, miliary tubercle may be found situated just beneath the epithelium. A chronic, diffuse, caseous form of tuberculosis is much more common. The entire cavity of the body of the uterus becomes filled with caseous material. The underlying tissue may be studded with tubercles, or irregularly ulcerated. Tubercles gradually form in the muscular tissue. As a rule, the cervical canal is not affected. Rarely, however, it is the only part of the genital tract diseased. Tubercle of the ovaries is rare, is always secondary, and almost invariably is part of a general disease. The number of recorded cases is small. It occurs in three forms—(1) Miliary tubercles on or just beneath the surface; (2) caseous deposits in the substance of enlarged or cystic ovaries; (3) tuberculous abscesses.

Tuberculous ulcers are rarely observed in the vagina. When they occur they are generally seated on the posterior wall, and are usually secondary to tuberculosis higher up. They have sharply-cut margins, and shallow floors, which are studded with granulations and covered with caseous material. Shallow ulcers of considerable size, with granular bases, have been observed on the vulva in a few instances.

Symptoms.—When secondary, the disease is usually quite latent, and not revealed by any symptoms. This is sometimes the case also when

the disease is primary. The symptoms are never characteristic, and, according to Whitridge Williams, " vary from those of simple endometritis and salpingitis to the most severe forms of pelvic abscess."

Diagnosis.—The discovery of the bacillus in the secretions, or of characteristic tubercles in the scrapings, is the only certain means of diagnosis. The rare form of cervical tuberculosis is very likely to be mistaken for malignant disease, and foul discharge and hæmorrhage may occur in one as well as in the other. The prognosis is always grave, on account of the danger of tuberculous disease manifesting itself elsewhere, especially tuberculous peritonitis and pulmonary phthisis.

Treatment.—Ulcers of the vagina, cervix, or vulva may be treated with topical applications, such as lactic acid, iodised phenol, or iodoform. Tuberculosis of the uterus may be dealt with by curetting and application of iodoform. In case of recurrence, vaginal extirpation of the uterus and appendages should be practised. If the disease is limited to the cervix, amputation may suffice. For tuberculosis of the tubes and ovaries their removal by laparotomy is indicated.

The Breast.

In many cases tuberculosis of the breast is associated with other obvious tuberculous lesions. Pregnancy, lactation, and mastitis are the chief predisposing causes. In some of the cases there has been a history of trauma. Out of fifty-seven cases collected by Scudder, only four were in men. Most of the cases occur between the ages of 20 and 35.

There are three possible modes of infection—(1) direct infection from without; (2) extension by contiguity; (3) metastatic tuberculosis, hæmatogenic, probably the most common form.

The disease occurs in two forms—(1) disseminated nodules; (2) a confluent mass. The first form is much the rarer. The nodules may vary in size from a hazel-nut to a walnut, and consist of caseous masses, with possibly softening centres. In the second form, there is a single tumour. This consists of a mass—sometimes hard, ill-defined, and bossy, sometimes more or less soft. It usually softens at the centre, and discharges through the skin, forming one or more fistulous sinuses, with indurated fungating edges. The discharge may contain caseous lumps. On section of such a tumour, there is found to be an irregular cavity, with diverticula, lined by a soft, downy membrane, surrounded by indurated greyish white tissue, containing groups of little opaque or semi-transparent nodules, with yellowish centres, or one or two larger masses. The tuberculous nodules develop round the acini and small ducts. The nodules have the ordinary structure. Giant cells are usually not numerous. Bacilli have been found in about half of the authentic cases.

Symptoms are not very characteristic. Pain, as a rule, is not a marked feature, although often present to some extent, and sometimes severe. The discovery of the disease is often accidental. The nipple is rarely retracted. The breast is usually small at an advanced stage, but in early cases may be enlarged. In nearly all cases the axillary glands are involved.

Diagnosis.—The usual association of the disease with tubercle elsewhere, the features of the tumour, the character of the discharge when there is a sinus, and the presence of bacilli in the discharge, or the result of

inoculation in guinea-pigs in doubtful cases, are the principal points which establish a diagnosis. Carcinoma is often with difficulty excluded.

Prognosis.—If the disease is secondary, its presence will probably not seriously complicate the progress of disease elsewhere. When primary, it slowly spreads locally, and implicates the axillary glands and sets up tubercle elsewhere.

Treatment.—When primary, and there is no evidence of secondary deposit in the internal organs, the tumour should be removed along with the axillary glands, if they are affected. When secondary, it is a question whether it should be left alone or not. Most surgeons are inclined not to interfere.

TUBERCULOSIS OF THE INTEGUMENTARY SYSTEM.

Tubercle, as it affects the skin, manifests itself under several distinct forms. Of these, by far the most common is lupus vulgaris. The other varieties are anatomical tubercle, verrucous tubercle, tuberculous gumma, and tuberculous ulcer.

LUPUS VULGARIS.

The now recognised position of lupus as a tuberculous disease was not established until the discovery of the tubercle bacilli in the lesions. Virchow described the lupus tissue as granulation tissue; Friedländer showed that it possessed all the histological features of tubercle—giant cells, epithelioid cells, and lymphoid cells; but Koch was the first, we believe, to demonstrate the presence of bacilli.

Ætiology.—Bacilli are invariably met with in the diseased parts, but they are extremely few in number, and their discovery requires great patience and the examination of many sections. Among perhaps fifty sections there may be only one containing one or two bacilli. The bacilli are found in the interior of, or in close proximity to, giant cells. They have never been discovered in the secretion or in the superficial crusts. Fragments of lupus tissue sown on serum have given rise to typical cultures of the tubercle bacillus. Inoculation experiments on animals have nearly always succeeded, when the inoculation has been intraperitoneal, and a large enough fragment has been employed. The paucity of the bacilli explains the failure of some observers who have attempted subcutaneous inoculations with minute fragments. It is unwarrantable to assume that the virulence of the bacillus is in any way attenuated.

It has been found extremely difficult, if not impossible, to produce tuberculosis in guinea-pigs and rabbits by the inoculation of superficial injuries to the skin; but the conditions of the skin are so different in these animals, from those in the human being, that little importance can be attached to this experimental fact. The situations of lupus are those where inoculation would be most likely to occur. A few cases where typical lupus has followed inoculation have been recorded. The lesions are very slow in their evolution. It has been already stated that the number of bacilli is extremely small. The reason of this is probably that the skin is a situation little favourable to the growth of the bacillus, on account of the close structure of the corium, and its relatively low and variable temperature.

Lupus abounds in populous districts, where other tuberculous affections

flourish. There is frequently a history of tubercle among the parents or other relatives of lupus patients. The disease has been observed in both parent and child, but such cases are exceptional, and there is nothing pointing to it being a hereditary affection.

The usual time of onset is during the period of adolescence or early adult life. It is rare in infancy, but it has been observed at the age of seven months. It is very uncommon in later adult life. Dr. Payne mentions as exceptional a case in a woman of 59. Women are more often affected than men.

A few cases have been recorded where there has been a history of trauma, such as a blow from a cricket-ball. There are also recorded cases of its occurrence in the tracts bored for earrings, and in the situation of tattooage. The latter have been cases of direct inoculation.

Association with other forms of tuberculosis.— The glands in relation with lupus patches, according to some observers, are rarely affected; according to others, they are not infrequently so. It is not uncommon for affection of the glands to precede lupus. Payne has stated that, in his experience, antecedent affection of the glands is a frequent if not usual cause of lupus under the lower jaw. Other observers have noted the frequency of lupus about the fistulous orifices of scrofulous abscesses. Payne found that about one-fourth of his patients had signs of tubercle elsewhere. Other observers give proportions varying from a fifth to two-thirds.

Morbid anatomy.—The characteristic of lupus tissue is the combination of necrosis with fibrous new growth. There is very little tendency to caseation, and it is very seldom that any considerable masses of caseous substance are met with. The tissue in an early stage may be seen to be composed of rounded nodules, discrete or confluent, consisting of groups of round cells, among which are embedded numerous giant cells surrounded by epithelioid cells. These are situated in the vesicular layer of the corium, and only extend to the upper layers when there is a tendency to ulceration. The papillary layer, as a rule, is not invaded by epithelioid or giant cells, although the papillæ may be swollen and more or less deformed and infiltrated with young cells. The epidermis is, as a rule, thickened, as regards both the horny layer and the Malpighian layer, including the prolongations which it sends between the papillæ. The hypertrophy of the interpapillary tissue may be so great as to suggest epithelioma. In other cases the epidermis may be atrophied.

Symptoms.—The most usual situation of lupus is on the face, particularly the cheeks and the nose, and less commonly the eyelids or the lips. Next in frequency come the extremities, then the buttocks and the trunk. The neck is occasionally affected, and very exceptionally the hairy scalp. The mucous membranes adjacent to the skin are sometimes involved. Of these, the nasal mucous membrane is the most commonly affected, next the conjunctivæ, etc. Most usually the lesion is single, and it is always so at first. Rarely there are multiple foci. In exceptional cases as many as fifteen lupus patches have been observed. Multiple patches generally appear early, so that, if a single patch has existed long, there is little likelihood of others making their appearance. The affected part is little painful or tender to pressure, and the patient is as a rule free from any symptoms. The lesion generally becomes aggravated in cold weather and improves in summer. Congestion or stagnation of the circulation makes it worse. The disease has but little influence on the general

health, although it has been observed that lupus patients are not long lived. The most characteristic feature of lupus, as observed clinically, is the presence of little nodules about the size of a pin's head, just beneath the epidermis. These nodules have a reddish or brownish yellow colour, and are semi-transparent. They have been compared to drops of apple-jelly or barley-sugar. In order to see them distinctly, it is sometimes useful to remove the hyperæmia of the epidermis by pressure with a glass. Although they can be plainly felt as well as seen, they are soft, and a needle or scarificator will pass into them with extreme ease. The nodules may be isolated, arranged in little groups, or they may be confluent. As a rule, they take several months to develop fully.

The affected part gradually increases in size, and often in an annular fashion. While spreading at the periphery, the lesion may be healing at the centre. In older lesions, such nodules as have just been described are only to be observed at the periphery.

The skin surrounding the affected tissue is generally slightly swollen and reddened from venous congestion. When ulceration occurs, the nodules caseate and soften, and migratory cells invade the corium. The epidermis exfoliates and ulcerates, and granulations develop on the floor. The floor secretes scanty thin pus, and the tubercles become covered with scales, crusts, or scabs. Just as in the case of tubercle elsewhere, the fibrous change may occur, and the tubercles gradually be transformed into fibrous cicatricial tissue. The same may take place after ulceration has occurred. As the result of this cicatricial contraction, the skin may be seamed and puckered and of a greyish white colour, as after a severe burn, and great disfiguration may result.

Lupus is extremely chronic in its course. It slowly advances, then becomes arrested or recedes, again to advance once more. It may finally cease to be active, leaving behind it cicatricial tissue.

OTHER FORMS OF CUTANEOUS TUBERCLE.

Tuberculous gummata have their seat in the corium or subcutaneous tissue, and are covered by red livid skin. They grow and, forming the so-called cold abscesses, soften or ulcerate, discharging a grumous, purulent secretion. They sometimes form in the course of the lymphatics. The pus contains few bacilli, but sets up tuberculosis in animals on inoculation.

Anatomical tubercle first appears as a red papule, becoming later a little pustule, which ulcerates and is covered with a yellowish crust. This gradually takes on a papillomatous character. Its most usual position is on the back of the fingers, hand, or forearm. It is not admitted that it is always tuberculous, but in the cases proved to be so the bacilli have been few in number, which may explain the failure to find them in other cases. A rare form has been described by Riehl and Paltauf, under the name of verrucous tubercle of the skin. This affects the same situations as the anatomical tubercle. It has been observed almost exclusively among adults who have much to do with domestic animals or their products. Unlike lupus, the lesion is situated in the more superficial layers of the cutis vera, the papillæ in particular being the seat of typical tubercles. Bacilli, moreover, are more numerous than in lupus. The lesions consist of roundish plates, from the size of a pea to a florin. They may be single or multiple. The centre is a projecting warty growth, divided by fissures and covered

with crusts. About this warty centre are numerous little superficial pustules, surrounded by infiltrated red skin. On squeezing the growth, pus exudes from innumerable little orifices. The lesion is slowly progressive up to a certain point, lasting from two to fifteen years. Like lupus, it may undergo cicatrisation.

Tuberculous ulcers of the skin are most frequent near the various orifices, mouth, anus, etc. They are almost always observed in persons already tuberculous, resulting from auto-infection. The ulcers are round, oval, or serpiginous. On the floor, tuberculous granulations are generally to be seen. In the neighbourhood, small pustules appear, which rupture and give rise to little round ulcers, and ultimately become continuous with the original ulcer. Bacilli are much more numerous than either in lupus or in the verrucous tubercle. On microscopical examination, typical tubercles can be seen in the derma.

Treatment.—In lupus, as in all forms of tubercle, constitutional treatment is valuable. Cod-liver oil, arsenic, creosote, etc., are useful, while, lately, thyroid gland appears to have been given with benefit. Tuberculin, both in the old and the new form, has produced temporary improvement, but does not appear in any way to arrest the progress of the disease. Local treatment has proved much more efficacious. What is aimed at by local treatment is the destruction of the diseased tissue, and the removal of all bacilli. The mode first introduced was the application of caustics, such as nitrate of silver, or caustic potash. Such applications are extremely painful, and it is difficult to limit their effects only to the diseased tissue. The best results have been obtained from thorough scraping, under an anæsthetic. The scraping may be followed by the application of some antiseptic, such as pyrogallol ointment (10 per cent.).

According to Unna, the best superficial caustic is the application of his salicylic and creosote plaster muslin, which may be obtained in three strengths, and in his experience no other preparation causes such a clean excavation of the lupus nodule. The strongest plaster should be used in the first instance, and may be kept applied for a week, unless there is much pain, when a weaker strength should be employed. Unna's zinc ichthyol salve muslin is a useful dressing, after treatment either with pyrogallol or salicylic acid and creosote. In all deep cases a caustic is necessary, and Unna prefers the chloride of antimony for the purpose. All the nodules should be touched with the following ointment:—Acid salicyl., liq. antimon. chlorid., extr. cannab. indic., of each 1 part; creosote, 2 parts; vaseline, 5 parts; lanoline, 10 parts. In older cases, with scattered nodules, double strength of salicylic acid, chloride of antimony, and cannabis indica may be employed. Several weeks of this treatment may be required. The other forms of cutaneous tubercle must be treated on similar principles.

The light treatment recently introduced by Finsen of Copenhagen, wherein, by means of special apparatus, the chemical rays of the sun, or electric light freed from the heating and illuminating rays, are brought to bear upon the diseased tissue, promises to be of great benefit if not actually curative in early and limited cases.

TUBERCULOSIS OF THE NERVOUS SYSTEM.

In addition to the acute form, tuberculous meningitis, already discussed at some length, we meet with tubercle in two chronic forms—chronic meningitis; tuberculous tumours.

CHRONIC MENINGITIS.

This is decidedly rare. The pia mater becomes thickened and nodular, and grey fibrous tubercles are adherent to its surface in the course of the vessels.

TUBERCULOUS TUMOURS OF THE BRAIN AND CORD.

Etiology.—These are usually met with in young people, four-fifths of the cases occurring under the age of 15. They are about twice as common in boys as in girls. They are generally found in association with tubercle in other organs, caseous bronchial glands, etc., although cases are sometimes met with where a tuberculous tumour is the only lesion present in the body.

Morbid anatomy.—They commonly vary in size from a pea to a walnut, but are occasionally much larger. Rarely they have been found invading the whole of a cerebellar lobe. They are rounded, well-defined bodies, firm and hard, of a yellow colour, consisting of uniform, opaque, cheesy matter, often surrounded with a softer pinkish grey translucent zone, in which sometimes separate tubercles can be detected. They seldom break down, but rarely the centre has been diffluent. Occasionally they have been partially calcified. They do not infiltrate the brain substance but compress it, and so cause it to atrophy. Sometimes they are single, but more commonly they are multiple. As many as twelve tumours, or even more, have been found in one case.

The cerebellum is more frequently affected than any other part, the cerebrum next, and then the pons. They are more common in the grey than in the white matter, and not infrequently abut on the surface, and become attached to the pia mater or even to the tentorium. They occasionally spring from the dura mater, and then compress the surface of the brain without invading it. They are usually of slow growth, and accordingly the symptoms, which are those of cerebral tumour, and need not be specially detailed here, come on very gradually. Occasionally meningitis supervenes, with its usual symptoms.

Tuberculous tumours of the cord are rare, but are more common in the upper part than in the lower. Occasionally more than one tumour is present in the substance of the cord. Tuberculous tumours growing from the dura-matral sheath are still more rare. Hale White has recorded a case of tuberculous growth between the dura mater and the upper dorsal vertebræ.

Diagnosis and prognosis.—Cerebral tumour in the adult is likely or unlikely to be tuberculous according as signs of phthisis are present or absent. In children, evidences of tubercle elsewhere are less likely to be present, and we must be guided by family history, situation of tumour, etc. A tumour growing rapidly and then becoming stationary is likely to be tuberculous. The duration may be short or long, a few weeks or a few years. Arrest of growth of a tuberculous cerebral tumour is not infrequent, and this is attended with relief to the symptoms, which, as far as they may be due to irritation and pressing, subside and may afterwards remain stationary for a long time. Lessening of the headache and passing off of the optic neuritis are favourable signs, while their persistence is unfavourable.

Treatment.—When we suspect the tumour to be tuberculous, we should endeavour to bring about arrest by treating the case on general principles, with good food, fresh air, etc.

HECTOR MACKENZIE.

LEPROSY.

THIS is an infective disease depending on the presence of a specific bacterium, *Bacillus lepræ*, in the tissues. It is characterised by recurring febrile attacks; macular skin eruptions; circumscribed granulomatous deposits in the skin, nerve trunks, and viscera; and by secondary ulcerations, local anæsthesia, and trophic changes. It runs a chronic course, and is rarely recovered from.

History and geographical distribution.—It is believed that leprosy was introduced into Europe from the East, *via* Egypt, some three or four hundred years before the Christian era. During the Middle Ages it overran the whole of the Continent, including Britain, and was probably more common in Europe at that time than it is anywhere, even in the East, at the present day. Presumably in consequence of compulsory segregation and isolation of the affected, and of the hygienic improvements coincident with advancing civilisation, leprosy has gradually, during the last four or five hundred years, diminished in Europe. As an indigenous disease, at the present day, it is quite unknown in Britain and in many other European countries. It still lingers, however, in certain limited districts in Norway and throughout the countries bordering on the Mediterranean. It is also found in one or two places in France, Germany, and Russia. In Asia, Africa, and the tropical parts of America it is still rife enough. Although unequally distributed in India, it is computed that in that country at the present day there are over 100,000 lepers; in China the number is probably larger. An important fact, as bearing on the question of infection, is the circumstance that within recent years leprosy has invaded countries which formerly were free from the disease.

Etiology.—The most important fact in the etiology of leprosy is the presence in the lepra tissues of a characteristic bacillus. This bacterium, discovered by Hansen in 1874, in its morphological and tinctorial characters closely resembles the *B. tuberculosis.* It differs, however, in one important particular: up to the present it has resisted all attempts at artificial cultivation. In consequence of failure in this respect, and of the non-liability of the lower animals to leprosy, the proofs that the bacillus is the cause of the disease with which it is uniformly, and, so far as known, solely connected, have not been established by the usual methods, and are to that extent incomplete. Nevertheless the association of the parasite with the specific lesions is so intimate, and the analogy between leprosy and the other disease mentioned—tuberculosis—so close in other respects, that there can be little doubt that *B. lepræ* and leprosy are related to each other as cause and effect, just as certainly as that *B. tuberculosis* is so related to tuberculosis. If this be granted, it follows that leprosy is a germ disease and therefore communicable and infectious. The facts of epidemiology are entirely in harmony with this conclusion. Thus leprosy mostly occurs in communities in which personal and domestic cleanliness are grossly neglected, and where the various members of the community and their fomites are in frequent and close contact. Moreover, although the disease runs in families, it appears only in those members who remain in the family home, and not in those who migrate at an early age to, or who have been born and lived in, non-leprous countries. The disease, therefore, is not hereditary, as was concluded at one

time. It appears in families because the various members living under the same conditions are exposed to the same opportunities of infection. These risks may be inherited; not so the bacillus. Another fact pointing to the infectiveness of leprosy is the gradual diminution of the disease in Norway since the isolation and segregation of lepers has been systematically enforced there. Its infective nature is further proved by the eccentric spread of the disease from foci; and by the fact that in recent times in the Sandwich Islands, in New Caledonia, and in other places previously exempt, leprosy, having been introduced from without, is now extensively endemic. Leprosy is not a powerfully infective disease. Certainly it is less so than tuberculosis; the two factors, individual receptiveness—possibly to some extent an inherited quality—and the presence of the bacillus, concurring less frequently than in the latter disease.

Occupation, social condition and race, seem to have no special bearing on liability to this disease, further than as affecting the chances of exposure to infection. It occurs at all ages, though, from the great length of the incubation period, it is necessarily rare in infancy and early child-hood. This incubation period is a very long one; its exact limits are difficult to establish, unless in very exceptional instances. There is no primary sore by which the date of infection can be fixed precisely. Two or three years may be stated as the average period; the extremes may be put at three months and thirty years.

Morbid anatomy and pathology.—The pathological element in leprosy is the leproma. This is an infiltration, consisting of an aggrega-tion of small cells, either in the deeper layers of the derma or in the nerves. In the ringed eruption presently to be referred to, the infiltration is more diffused and does not produce a definite circumscribed tumour.

The section of a leproma of recent origin is white, glistening, and juicy; if more mature, it has a brown tinge. The cells of which the infiltration is mainly composed contain innumerable bacilli; some cells three or four, others many, some being literally crammed with the parasites. According to Unna, the bacilli may be found free in the lymph spaces. If the juice of one of the cutaneous nodules is expressed and placed on a slip and suitably stained, the bacilli can readily be made out. Examined in the fresh state, they exhibit considerable activity. In the older lepromas, globular, dark masses, known as "globi," are found. They give the brownish tinge to the section, and are believed by Hansen to be made up of the remains of degenerated bacilli. Leprotic infiltration occurs in the liver, spleen, and, from an early stage of the disease, in the testes. The macular eruptions, the prodromal and febrile phenomena of leprosy, are to be explained by the presence in the blood of a bacillus-evolved toxine; the paretic and trophic lesions in nerve leprosy are attributable partly to nerve degenera-tion caused by the pressure on the nerve tubules by lepromatous infiltra-tion in the neurolemma, partly also, according to some recent investigations, to leprotic invasion of the nerve terminals.

Symptoms.—In the majority of cases there is a distinct prodromal stage, lasting for weeks or months or even for years, during which the patient suffers from recurring febrile attacks, headache, languor, depression, sleeplessness, sometimes profuse perspirations, neuralgia, various paræs-thesiæ, rheumatic pains, and so forth. In a few instances there are no prodromata.

After a febrile attack of greater severity than usual, a macular eruption, which may be profuse, or which may be limited to one or two

spots, appears. The maculæ vary in size, in shape, and in colour as well as in number. Generally they consist of very slightly raised erythematous patches, darker in the centre, and shaded off at the periphery. Sometimes they are pigmented; sometimes they are vitiliginous; sometimes they are barely half an inch in diameter; sometimes they are larger than the palm of the hand. Sometimes erythematous patches become pigmented; or they may assume a ringed appearance, being pale and somewhat depressed at the centre and dark red at the narrow, slightly raised ring forming the periphery. The earliest spots tend to disappear; but, with recurring attacks of fever at longer or shorter intervals, new maculæ are formed which progressively tend to become more permanent, to be more markedly anæsthetic, more pigmented, or more vitiliginous. The hair on the affected areas falls out, and the sudoriparous glands become atrophied.

The face, particularly the superciliary region, is a favourite situation for the macular eruption; but trunk and limbs also are usually more or less involved. As a rule, the hands and feet at this stage are exempt. A curious fact is that the hairy scalp never becomes the seat of any of the specific leprous lesions, either early or late.

After a longer or shorter time, the disease enters on a further stage, and a characteristic granulomatous growth or deposit—the leproma—is formed in the skin, in the nerve trunks, or in both. If in the skin, what is known as nodular (tuberculous) leprosy; if in the nerve trunk, what is known as nerve (anæsthetic) leprosy; if in both, mixed leprosy is produced.

Nodular leprosy.—In this the prodromata are often well marked, but the macular stage may be slight or altogether absent. From time to time, usually accompanied by marked febrile movement, purplish (later becoming brown) thickenings of the skin, leading to pronounced boss-like nodules or plaques, appear. These thickenings, which are firm, rounded, and involve the derma, are in some instances more or less permanent; in others, after a time they may be absorbed; in others again they may ulcerate. The face, ears, neck, arms, hands, thighs, legs, and feet, but especially the face, are favourite situations for these nodules. In the case of the face, when the thickening is of great extent, the features are rendered grotesque and repulsive in the extreme. The skin of the forehead and cheeks is thrown into heavy folds, and the nose and lips are thickened and broadened out. This appearance is appropriately called "leontiasis." As the disease progresses, the conjunctiva, and the mucous membrane of the nose, of the mouth, and of the larynx, are also involved. Destruction of the cornea, fœtid discharge from ulceration of the nostrils, ulceration about the mouth, and stenosis of the larynx—one or all of them may ensue. Thus, in time, the patient loses the senses of taste, of sight, and of smell, and speech may be reduced to a husky whisper. Later on the nerve trunks are also involved, and anæsthesia and trophic changes similar to those in nerve leprosy ensue. Ulcers form in the leprotic patches on the limbs; fingers and toes are lost from atrophy or ulceration. There may also be swelling of the abdomen from leprotic deposit in the liver, diarrhœa from amyloid disease of the bowel, septic conditions from the ulcerations. Phthisis may ensue, or the patient may die from slow exhaustion, or from some form of intercurrent acute disease. Sexual power, owing to nodular deposits in the testes, is early lost.

Nerve leprosy.—The characteristic feature of this type is the deposit of leprous tissue in the nerve trunks, leading to loss of function and

secondary trophic or inflammatory changes in the corresponding nerve areas.

After the prodromal and macular stage, well-marked numbness or muscular weakness of a hand or foot, sometimes preceded or accompanied by severe neuralgic pains, tingling, and other paræsthesiæ, generally sets in. On examining the nerve trunks where superficial, or where they lie over bones, particularly the ulnar nerve at the elbow, firm fusiform thickening is readily made out. By degrees the anæsthesia in the implicated area becomes absolute, the muscular wasting complete. Other trophic changes also ensue; the hair of the part drops out; the sweat glands atrophy; bullæ may form; or changes in the pigmentation may supervene. Ulcerations are common, particularly in the hands, feet, fingers, and toes; perforating ulcer of the foot is frequently seen. The fingers and toes may perhaps become gangrenous, or the phalanges may undergo slow interstitial absorption. Deformities from loss of parts or from muscular atrophy result. The motor and sensory nerves of the face may be similarly affected, the muscles of expression becoming atrophied and paralysed. Thus the upper eyelid may droop, the lower eyelid become everted, and the eye can now no longer be closed or moved. As a consequence, conjunctivitis and, later on, cornification of the conjunctiva and cornea ensue. The muscles about the mouth and those of mastication and articulation may also be similarly affected; the saliva then dribbles from the mouth, chewing and deglutition are difficult; speech is husky and inarticulate. Ulceration of the larynx is common, giving rise to aphonia and difficult breathing. By degrees the functions of the muscles perish one after another, until the patient becomes completely helpless, unable to move, and with perhaps only one of his senses, that of hearing, intact. Diarrhœa, phthisis, bronchitis, or some other intercurrent disease may supervene, and be the immediate cause of death.

Mixed leprosy.—In this, nodulation and nerve lesions supervene one on the other, or they may concur from the onset.

Diagnosis.—The presence of well-marked anæsthesia in a skin lesion is distinctive of leprosy; equally so is the discovery of the bacillus in the tissues, expressed juices, or discharges of a cutaneous thickening, ulceration, or other skin lesion. Falling of the hair and absence of perspiration in an anæsthetic spot, thickening of nerve trunks concurring with skin eruptions and trophic lesions, are also distinctive.

Prognosis.—Nerve leprosy lasts longer than the nodular form; the average for the former being eighteen, for the latter eight to nine years. Cases of the nodular variety sometimes run their course in one or two years. Recovery from leprosy is very rare indeed. It is not unusual to see nerve leprosy arrested for a time, and the disease drawn out for twenty or thirty years even, the patient dying of some other disease before the leprosy can be said to have run its course.

Treatment.—The hygienic conditions should be the best obtainable. Frequent bathing, warm clothing, good food, light occupation, a dry, bracing climate, tonics, cod-liver oil, and everything which may improve the general health, should be had recourse to.

In the treatment of leprosy, many drugs have been employed in the hope that they possess a specific influence on the disease. A genuine specific has yet to be discovered. Chaulmugra oil (*oleum gynocardium*), in doses of from two up to forty drops, according to tolerance, three times a day, in capsules or emulsion, is a favourite drug in English practice.

Unna gives ichthyol internally in increasing doses, treating the surface lesions at the same time with pyrogallic acid (10 per cent.), or chrysophanic acid (10 per cent.) in lanoline ointment. Crocker has recently recorded two encouraging cases treated by hypodermic injections of one-fifth of a grain of mercury bichloride, administered at suitable intervals. Danielsen gives the salicylates in increasing doses, four times a day, beginning with 15 grs., for six months or a year, and claims that this treatment is effective if instituted in the early stages.

Lepers ought not to be allowed to mix freely with the general population, more especially during the ulcerative stages of the disease. To any given individual the risk of infection is small, but the chance of some individual in the community becoming infected by a leper associating freely with its members is considerable. A system of isolation and segregation—such as is practised in Norway—in which the rights of the leper as a human being are not altogether sacrificed to the interests of the rest of the population, is not only from an ethical standpoint the right system, but practically, since it is not repellant and so does not lead to concealment, is the best and most effective.

In vaccinating children in leprous countries, great care should be exercised in selecting a vaccinifer free from the slightest suspicion of leprosy. Similarly, in such countries, care should be exercised in the selection of wet nurses and domestic servants.

<div align="right">PATRICK MANSON.</div>

ACTINOMYCOSIS.

A SPECIFIC infective disease, due to the presence in the system of the ray fungus, or *Actinomyces bovis*, and attended by the formation of chronic abscesses, or tumour formations of granulation tissue.

History.—This disease was first recognised as having a parasitic origin in cattle, by Bollinger, in 1876. It occurs most frequently in oxen, where it gives rise to what is known as "wooden tongue"; but also affects swine and other animals. Since attention has been directed to the subject, a considerable number of cases have been observed in the human subject, by Israel and others.

Etiology.—The disease is undoubtedly due to a parasitic fungus, which is usually regarded as a species of cladothrix; but its exact botanical position and life-history have not yet been properly worked out. Great difficulty was at first experienced in cultivating the organism, and when this was accomplished its appearance in artificial cultivations was so different from that in the animal body, that doubt arose as to whether it was the same organism. The disease does not appear to be usually contracted from other cases of the infection, either in man or animals; but both man and animals appear to be infected from the same source and in the same manner, probably by means of certain varieties of grain on which the fungus grows. The disease is usually localised in, and is acquired through, the respiratory or alimentary tract.

The organism, as found in the tissues, consists of a series of short threads arranged in a radiating manner, many springing from a common centre. It is from this radiating arrangement that the fungus has been called the ray fungus, or actinomyces. The individual clumps are of small

size, and not visible to the naked eye ; but are usually united into larger masses, and form small yellow-coloured granules in the discharges and new formations, which form a characteristic indication of the disease. The organism may be most easily recognised by staining with gentian-violet, according to Gram's method.

Morbid anatomy and pathology.—The organism, wherever deposited, gives rise to irritation of the tissues, which is followed by small-celled infiltration, accompanied not unusually by the formation of giant cells. The character of the process appears to depend on the local resistance of the tissues, and probably also on the nature of the infecting organism. Where the resistance is great, inflammatory reaction occurs in the neighbourhood of the new formation, and this tends to develop into connective tissue, especially at the periphery, and thus arrest the further progress of the disease. Where the tissues are more susceptible, the small-celled infiltration spreads rapidly, the tissues undergoing necrosis. There is no tendency to develop granulation tissue, nor to form a bounding zone of connective tissue, although the parts first affected form finally dense scar tissue. The tissues affected ultimately undergo fatty degeneration and liquefaction, with the formation usually of creamy pus, in which the characteristic organisms are to be found.

Symptoms.—The symptoms resulting from the development of actinomycosis are those which attend on the formation of a chronic tumour, which ultimately bursts in the direction of least resistance, and discharges its contents, and then tends to cicatrise. This is usually accompanied by little pain or constitutional disturbance, owing, no doubt, to the chronic character of the process. The symptoms may, however, be much more acute, and simulate pyæmia, which may be ascribed to the entrance of pyogenic organisms.

When the jaw or pharynx is affected, the tumour gives rise to those symptoms due to its mechanical interference with the tissues involved. The disease may spread to the thoracic or abdominal organs, or may even primarily affect these, and in each case gives rise to its appropriate symptoms.

Diagnosis and prognosis.—The diagnosis must depend upon the chronicity of the affection, and the discovery, if possible, of the characteristic organism in the discharges. It may be distinguished from a sarcoma frequently by the fact that the enlargement of the lymphatic glands is usually absent. The disease is sometimes very chronic, and where it can be extirpated surgically the prognosis is good. Spontaneous recovery has not, however, been observed.

Treatment.—The only treatment available till quite recently was that of extirpation by the knife or sharp spoon, but the very favourable results obtained by the use of iodide of potassium in cases of this disease in cattle, warrant us in expecting similar results in the human subject. It should be noted, however, that the character of the tissue reaction in the human subject would suggest that in this case the disease is more virulent than in the case of animals, and that accordingly, perhaps, less marked results may be expected from this treatment.

<div align="right">G. E. CARTWRIGHT WOOD.</div>

HYDROPHOBIA—RABIES.

An acute specific disease, the causal agent of which is still unknown, which affects chiefly the central nervous system, and which was, until the introduction of the Pasteur treatment, almost invariably fatal.

History.—The microbe associated with this disease has not yet been isolated; but as it comports itself in all respects like one due to a living organism, there can be no question as to its causation. Pasteur's experiments, which showed that the virus might be intensified by passage through certain species of animals, and attenuated by inoculation into another species, and that animals can by a process of vaccination be rendered insusceptible to the most deadly form of inoculation, established definitely that the disease was due to a living microbe. Although unable to demonstrate the cause of the disease, Pasteur continued his investigations, in hopes of discovering a method of curing the disease, and in 1885 employed his process on Joseph Meister with a successful result. The treatment consists in the subcutaneous injection of emulsions of the spinal cords of rabbits which have been killed with the most intense virus of rabies. It had been found that when the spinal cord was retained in a dry atmosphere, at 22° C., for fourteen days, it had become quite inactive; while, when exposed for shorter periods, the virus was correspondingly more active. The first injections consist of emulsions, which have been exposed for fourteen days, but those of more recent date are afterwards employed until a virus which has been treated for only three days is used for the emulsions. The amount introduced, and the rapidity with which the cords of different strengths are made use of, are varied according to the character of the case under treatment. The success of this treatment in the case of rabies depends on the fact, first, that the disease has a long incubation period; secondly, that we are able to recognise the probability of inoculation of the disease at the time of its occurrence. Under these conditions, we anticipate the development of the disease by inducing a condition of immunity or greater resistance of the tissues by the introduction of the specific products of the virus. The immunity thus induced is only a relative one; so that the potential resistance of the tissues is increased to such an extent that the virus originally introduced acts now merely as a vaccine, inducing in a successful case of treatment little or no disturbance of the general health. This is indicated by the fact that the cases where the treatment has failed have been cases brought under treatment at a late stage, or those resulting from the worst species of bites, such as those occurring on the face and caused by wolves. It has been experimentally shown, for many bacterial diseases, that the introduction of a vaccine exerts no influence on a disease which has already begun to manifest itself, and that frequently the disease is even more deadly than normal, unless a certain definite period has been allowed to elapse between the process of vaccination and the control inoculation of the virulent virus. We can thus understand that, where too short a period for the induction of immunity elapses between the injections and development of the disease, to allow of the acquired tolerance of the tissues keeping pace with the advance of the disease, the virus no longer manifests itself as a vaccine, but develops the usual symptoms of the disease, probably almost uninfluenced by the treatment to which the patient has been subjected. In addition to the Pasteur treatment, more recently a method analogous to that introduced by Behring for diphtheria

and tetanus, in which antitoxic serums are used to antagonise the virus, has been suggested, in which antirabic serum is used to combat the disease ; but the results at present to hand must be regarded as entirely tentative.

Etiology.—This disease is in man invariably the result of inoculation with the poison of rabid animals, which commonly occurs as the result of a bite. In most cases this disease is contracted from dogs, but cats, wolves, and foxes may also transmit the disease; it has even been contracted from the infection of a wound acquired during the dissection of a rabid animal. Other animals, such as cows, deer, and horses, may become rabid, but are not of importance as regards setting up the disease in the human subject. Statistics seem to show that bites from the wolf and the cat are more dangerous than those from the dog, and this appears to be due to the poison being more active in these animals, but may also be attributed to the bites in these cases being more severe and frequently multiple. The saliva is the only secretion in which it has been proved that the poison is present. Only a certain proportion of those bitten by a rabid animal are affected by the disease; and although the figures quoted on the point vary greatly, it is probable that at least two-thirds of those exposed to the infection may escape. In this respect, however, the locality of the bite and its extent and depth exert great influence; thus a bite incurred through the clothing is probably much less deadly, owing to most of the virus being wiped off the teeth, which would account for the relative greater danger from wounds on the uncovered parts, such as the face and hands. There seems, however, no doubt that bites on the face are not merely more apt to give rise to the disease, but are, as a rule, more acute. This has been ascribed to the fact that, as the virus travels along the nerve trunk to the central nervous system, in the case of the face the path is much shorter than where one of the extremities has been the site of inoculation. Where the bites are multiple, the probability of infection, and of an acute type, are naturally increased.

The usual period of incubation in the human subject is six or seven weeks, but, on the other hand, cases have been recorded where symptoms have supervened within a week, while they may not develop till as late as two years (Horsley). These variations are no doubt to be accounted for by the amount of the virus originally introduced, its activity, the nature and extent of the wound, and the susceptibility of the individual affected.

Morbid anatomy and pathology.— The morbid changes observed consist practically of evidences of hyperæmia and congestion in the central nervous system. In special places, local congestion with migration of leucocytes into the perivascular lymphatic spaces and the interstitial neuroglia, along with slight extravasations of blood, may be observed. These are said to be found chiefly in the neighbourhood of the medulla oblongata. Congestion and sometimes even hæmorrhages from the mucous membranes may also be found in the fauces, pharynx, œsophagus, and stomach.

Symptoms.— The wound usually heals without developing any unusual symptoms, and the general health remains apparently unimpaired during the period of incubation. Occasionally the wound becomes irritated, or even undergoes inflammation, as the acute symptoms set in. The earliest symptoms are usually malaise, disturbed sleep, and a difficulty in swallowing fluids. The pulse is quickened, sometimes becoming very rapid, and the respirations are hurried and shallow, and these

symptoms are succeeded by a general hyperæsthesia. As the disease progresses these symptoms become much more marked. The patient suffers from great mental excitement and even from hallucinations. The mouth and fauces become congested, and the patient ejects with great difficulty and much noise thick tenacious mucus. The attempt to swallow is attended with the greatest agitation, which induces spasmodic contraction of the muscles of deglutition, followed by contraction of the respiratory and abdominal muscles, in consequence of which the respiration is suspended, and the patient may die from syncope during one of these attacks. The spasms of the muscles may then become general and convulsive in character, and excited by the slighest external cause. The patient usually succumbs finally to exhaustion, and does not exhibit the typical paralytic stage exhibited in the dog and other animals.

Diagnosis.—In the recognition of the disease, the history of the case as regards the condition and source of the bite are usually sufficient to clear up any doubts. The early symptoms may be stimulated by mere hysteria, but the untypical character of the respiratory symptoms usually suffices to distinguish in these cases. This disease has sometimes been confounded with tetanus, which may also occur as the result of a bite, but the much shorter incubation period of the latter, the character of the spasm, and the absence of the mental anxiety present in the former disease, suffice to distinguish them.

In consideration of the anxiety to which a person bitten may be exposed, owing to the long period of incubation which may supervene before symptoms develop, it is desirable that, wherever a person has been bitten by an animal suspected to be suffering from rabies, that the question should be definitely settled by the inoculation of animals. This is done by inoculating a rabbit under the dura mater with a small proportion of the medulla of the suspected animal, when, in the course of two or three weeks, the animal should evince symptoms of paralysis, forming what is known as dumb rabies. In the case of negative result, all anxiety as regards the consequence of the bite are at once obviated.

Prognosis.—Hydrophobia was practically a fatal disease until the introduction of the Pasteur treatment, but where this has been commenced within six days of the bite the prevention of the disease is practically certain. The later the period after the inoculation of the virus that the patient is brought under the treatment, the less certain is the result. It must also be borne in mind that bites on the head, or those acquired from cats or wolves, where the poison is more virulent, are much more dangerous and less susceptible to Pasteur's treatment than others.

Treatment.—Prophylaxis.—Until recently, our only method of combating the disease was to stamp out or prevent the spread of infection in dogs, from whom the disease is usually contracted in this country. This was done (1) by muzzling all dogs, and (2) by destruction of all ownerless dogs. The enforcement of this regulation produced a steadily decreasing number of cases, but on the relaxation of the order the figures then began to rise slowly but steadily, until it was again enforced. This indicated quite clearly that the disease might be probably practically extirpated, if proper care were exercised for a sufficient period of time.

Local treatment.—The wound may be treated with strong carbolic acid, and then, if possible, excised; but these surgical measures cannot however be relied upon.

Pasteur treatment.—In every case where a patient has been bitten

by a dog, which there are good reasons to suspect of being rabid, recourse
should be had to this treatment, since it has been shown that a previous
mortality of 15 per cent. has been reduced by its means to less than 1 per
cent. Where the disease has already manifested itself, we can only alleviate
the symptoms by having recourse to large doses of powerful narcotics.

<div align="right">G. E. CARTWRIGHT WOOD.</div>

ANTHRAX.

AN acute specific infective disease, due to the introduction and multi-
plication of the *Bacillus anthracis* in the system.

History.—It is one of the most fatal and widespread diseases which
affect cattle, occurring frequently, as it does, in both the New and the Old
Worlds, where it is known as splenic fever, from this organ being as a rule
markedly affected. Among the domesticated animals usually affected are
horned cattle, horses, sheep, and swine. It may be said, indeed, generally,
that the Herbivora are susceptible, while, on the other hand, the Carnivora
are as a rule more refractory; thus many wild animals, such as deer,
buffaloes, camels, and elephants, are subject to the disease. This disease is
of special interest to us, as it was the first disease in which a microbe, as
a causal agent, was definitely demonstrated, and in which, still later, the
possibility of attenuating the microbe, so that it might be used as a vaccine
to protect against subsequent infection with the disease organism, was
first established. Indeed, most of the important advances in our know-
ledge of bacteria were made by investigations carried out with this organism.
As early as 1849, Pollender observed the occurrence of short rods in the
blood of animals which had succumbed to the disease; the relation of these
rods to the disease was, however, only established much later by Davaine
and Pasteur. To Koch, however, the credit is due of furnishing the com-
plete proof, by cultivating the organism on artificial media, and infecting
susceptible animals from cultures which had been carried on for many
generations outside the animal body. He was also able to work out in
great part the life-history of the bacillus and its relation to the disease.

The organism consists of rods, usually about 1 μ in breadth, and varying
extremely in length, from short rods (3 μ) to long filaments (20 μ).
These rods are easily destroyed by heat, antiseptics, and many conditions
—such as drying—to which they are naturally exposed in nature, so that
one might expect that the disease would tend to disappear. Koch was
able to show, however, that under favourable conditions very resistant
spores were formed, and that these are, at any rate usually, the origin of
the disease in cattle, which is the result of the ingestion of the spores in
the food, the bacilli themselves being unable to effect this, owing probably
to the antiseptic action exerted by the gastric juice. These spores, how-
ever, are only produced under certain special conditions of temperature
and presence of oxygen. They do not appear to be usually formed at a
temperature lower than 24° C., and only then under conditions which
permit of free access of oxygen. Spores are never formed within the
animal body, so that the disease is usually spread by the discharges from
the intestine and bladder giving rise to the formation of spores after being
evacuated where the external conditions, especially those of temperature,

are favourable. If the animal, however, is opened, the blood which is shed and the organs which are exposed to the air, should they contain the bacilli, under favourable conditions rapidly gives rise to spores. We can in this way readily understand how a locality where a case of anthrax has occurred, may become infected with the spores, and in this way the disease remain endemic and continue to give rise to the disease for a long period of time. The influence of temperature in allowing the disease to become endemic is shown by the fact that it occurs in this form in France, Germany, Austria, and Russia, whilst in Britain in most cases the germs seem usually to have been imported either with fodder or on dried hides.

The symptoms occurring in this disease were at one time ascribed to the mechanical influence exerted by the presence of the bacilli, and even to their producing directly a form of asphyxia, but these are now by common consent ascribed to the toxic products secreted by the organism. By cultivation of the organism in broth containing fibrin, E. H. Hankin obtained an albumose which was able to confer immunity upon animals against subsequent inoculation with the living organism. Almost simultaneously Sidney Martin showed that the *Bacillus anthracis*, as the result of its growth on alkali albumin, produced a proto-albumose, a deutero-albumose, and a toxic alkaloid, and that these bodies were able to account for the symptoms occurring in this disease. The absolute proof of this conclusion he furnished by the separation of these substances from the organs of animals which had succumbed to the disease. The alkaloid was much the most active poison, and apparently gave rise to most of the acute symptoms met with in this disease.

Etiology.—The disease is acquired in man always directly or indirectly from animals. The local form, which occurs usually in butchers, is acquired directly by the introduction of the bacilli through a wound, when dressing the carcase of an animal affected with splenic fever. It may be also acquired indirectly by wool-sorters, tanners, and those engaged in occupations where they come in contact with the hides or hair of animals, by the entrance of the spores through a wound or scratch, although this may occur without visible injury to the skin. It has been suggested that the bites of flies which have settled on the carcase may also convey the disease. The internal form of anthrax, where the disease originates from the intestinal canal or through the lungs, is due to the inhalation or ingestion of spore-bearing material.

Morbid anatomy and pathology.—In malignant pustule we have an inflammatory exudation under the skin, rapidly extending into the deeper layers, which is accompanied by hæmorrhages, due to the rupture of the vessels. The cells at the same time undergo a process of coagulation necrosis, and the central portion, which acquires a black colour from the effused blood, forms the eschar which is so typical of this form of the disease.

In the pulmonary form the lungs are usually collapsed, but the most characteristic feature is the presence of clear serous fluid in the pleural and pericardial cavities, although there may be no signs of inflammation of the serous membranes. There may be small patches of broncho-pneumonia scattered throughout the lungs, and small hæmorrhages, but it is much more usual to find the mucous membrane of the trachea and upper bronchi swollen irregularly, and certain patches specially affected where small hæmorrhages appear to have occurred. The bronchial and mediastinal glands are very much enlarged, and filled with hæmorrhages. The

pleural and pericardial effusions which are so characteristic of this disease are probably due to the enlarged glands pressing on the blood vessels, or, as has been suggested by Greenfield, to the rapid obstruction of the lymph channels in the glands interfering with the lymph absorption. The collapse of the lungs, on the other hand, may be ascribed to the swollen condition of the air passages, offering an obstruction to the entrance of air.

Symptoms.—The symptoms and course of the disease vary greatly in different cases. The various forms are usually described under the region of the body primarily affected: First, the external, commonly known as malignant pustule; second, the internal, which includes the intestinal, and the pulmonary. It must be borne in mind, however, that in either of these forms there may be little or no local manifestation, the disease at once becoming general, and constituting what is practically a septicæmia.

External.—The first sign of this form of the disease, commonly known as *malignant pustule*, consists usually in the appearance of a small red papule, which rapidly extends in a few hours into a large red swelling. On the summit of the swelling a small raised papule then forms, which becomes vesiculated, and ultimately forms a dry scab on the surface, and round this dark eschar there occurs frequently a circle of vesicles, while the swelling itself becomes greatly indurated, and usually continues to spread; at the same time, the poison is taken up by the lymphatics, and the glands enlarge. The formation of the pustule is sometimes wanting, and the nature of the swelling at the same time is different, assuming more an œdematous character, while the lymphatics are not affected to the same extent. This form is usually much more fatal than the other, the disease apparently becoming much more rapidly generalised and invading the whole system. The course of the disease and the nature of the symptoms vary greatly, being dependent, no doubt, on the quantity of the infective agent primarily inoculated, the virulence of the material, and the constitutional peculiarities of the person affected. These factors determine the time which intervenes before the carbuncle makes its appearance, its character, progress, and tendency to remain localised or to invade the system. Where the local reaction is great, we should expect, from our experimental knowledge of the disease, that the tissues of the affected person were exhibiting a certain resistance to the infection—in fact, attempting to localise it; while, on the other hand, where little reaction, or only œdema is to be observed, no resistance is offered to the disease becoming generalised and running a rapid course. It is due to this fact—that the disease is localised in the earlier stage—that the surgical treatment of malignant pustule is so successful; as even where the whole of the infective material may not be removed, by reducing the amount of the virus present we tend to reduce the quantity coming into action to that which would constitute a vaccine. The carbuncle gives rise to little pain, and in the early stage the only constitutional symptom is a feeling of general malaise; but as the poison becomes absorbed into the system the temperature may rise to 102° F., or even 104° F.

Internal.—The forms of internal anthrax vary greatly, and this is due to the fact that the disease may give rise to little or no local manifestations at the point of entrance, similar to the œdematous variety of the external form of the disease; while, on the other hand, it may give rise to local lesions in the intestines or lungs, corresponding in character to the ordinary malignant pustule. The onset of the disease is often sudden, but sometimes is preceded by premonitory symptoms of depression, pains in

the limbs and back, and cold perspirations. This is succeeded by extreme prostration, which rapidly terminates in collapse. The temperature varies greatly, and may be very high or only slightly above the normal.

Intestinal.—In this form we may have, in addition to the general symptoms, others indicating the special system affected: thus pain in the abdomen, vomiting, diarrhœa, with or without bloody stools, and bleeding from the pharynx, may sometimes be noted. The glands in the neck are also sometimes enlarged.

Pulmonary.—In this form, commonly known as woolsorter's disease, the symptoms of acute bronchitis or pneumonia may be more or less present, but the local signs of the disease are out of all proportion to the constitutional symptoms and effects.

Diagnosis.—In the early stage, the external form can only be recognised from the history of the case indicating exposure to the contagion. In the later stage, the malignant pustule is very characteristic, and, in case of doubt, could be recognised bacteriologically, or by the inoculation of mice or guinea-pigs. In the œdematous form the signs and symptoms are of little assistance, and we should have to rely upon the bacteriological diagnosis to come to a definite decision. In the internal form of anthrax the diagnosis must always be attended with the greatest difficulty, and we must rely chiefly on the possibility of the patient having been exposed to the infection.

Prognosis.—In the case of external anthrax, where the patient is brought under early treatment, the majority of the cases recover. The œdematous form is, however, usually rapidly fatal. In all cases of internal anthrax, on the other hand, the prognosis must be exceedingly unfavourable.

Treatment.—External anthrax should be at once treated surgically by excision, if possible, and cauterisation with pure carbolic acid. Where the carbuncle is very large, crucial incisions should be made, and the wound again cauterised with strong carbolic acid. In these cases 5 per cent. carbolic acid has been injected into the surrounding tissues apparently with advantage. It is hardly necessary to say that all discharges should be most carefully disinfected. In internal anthrax no special treatment at present known appears to exert a beneficial influence.

G. E. CARTWRIGHT WOOD.

GLANDERS.

A CONTAGIOUS febrile disease, communicated to man from the horse, ass, or mule, due to the multiplication in the system of the glanders bacillus (*Bacillus mallei*), and characterised by specific inflammatory lesions of the nasal and respiratory mucous membranes, the lymphatic vessels, and glands.

History.—This disease has long been recognised as a common and very deadly affection for horses, and up to quite recent times was described as two distinct affections, according to the nature of the characteristic lesions. In those cases where the nasal and respiratory mucous membranes are most obviously affected, the disease was termed glanders; while in those cases in which the lymphatic system was chiefly affected the disease was termed farcy. The two sets of lesions are, however, usually associated, or occur in different stages of the disease, and no reason now exists for

regarding them as distinct, since they are both due to the presence of the same organism. It has, in addition, been proved that the same virus may give rise to the two sets of lesions, when inoculated into different horses. As early as 1869, Chauveau suggested that the virus must be particulate in its nature; but it was only in 1882 that Löffler and Schutz described a definite organism—the glanders bacillus—as occurring in the infected tissue. This organism they were able to cultivate, on artificial media, outside the animal body, as a pure culture with which they could reproduce the disease in other animals.

Etiology.—Glanders, when occurring in man, is due to inoculation with the virus of the disease, usually directly from a horse, but sometimes from man, and even from artificial cultures used in laboratory experiments. It is met with most frequently among those employed in the care of horses, and its mode of communication can in most cases be easily traced. The virus usually finds an entrance through some breach in continuity of the skin or mucous membrane, which has come in contact with discharges from the diseased surface. It is, however, possible that infection may occur through the healthy mucous membrane. The glanders bacilli are small slender rods with rounded ends, somewhat shorter and thicker than the tubercle bacillus. They occur either singly or in pairs, but never in long threads, and are non-motile. The bacilli are not so readily demonstrated as in many other diseases, owing apparently to the fact that they absorb the stain readily, but give it up as readily during the process of decolorisation. They can be stained in aniline gentian-violet or carbol-fuchsin, and then slowly decolorised in a 1 per cent. solution of acetic acid and water, to which a small quantity of tropæoline has been added. The bacillus will not grow at a temperature under 25° C., or over 42° C. When inoculated on glycerin agar, and incubated at 37° C., in three or four days a clearly-defined whitish, moist, shiny coat forms along the tract of the inoculation. The organism grows well on potato as a thin amber-yellow transparent film, which ultimately takes on a reddish brown colour. This appearance is very characteristic, and serves to distinguish it from most other organisms. Among the smaller animals, field-mice, guinea-pigs, and cats are most easily affected, and may be used for purposes of diagnosis. The ordinary anti-septics, such as carbolic acid and Condy's fluid, in the usual dilutions, rapidly destroy the virus. It is rather surprising that, although this organism does not form resistant spores, still, when maintained in a dry state, it may retain its activity for almost three months.

Morbid anatomy and pathology.—This disease is characterised by the formation of swellings and nodules in the skin, mucous membranes, lymphatics, and internal organs. These nodules consist of a deposit of granulation tissue, which in the acute form passes on into pus formation, and frequently present the appearance of a pyæmia; while in the chronic form they develop more in the direction of caseation. The deposits tend to break down, so that ulcers form, which present a great tendency to spread. These ulcers occur frequently on the nasal and respiratory mucous membranes, but also on the skin. The characteristic bacilli are to be found in the nodules, and can be recognised by appropriate staining.

Symptoms.—The period of incubation varies greatly, from a few days to several weeks, and it may be stated generally that the severity of the case varies inversely with the length of this period. This variation is no doubt due to the quantity of the virus primarily introduced and its virulence, on the one hand; while the nature and the condition of the

tissue inoculated, as well as the natural susceptibility or insusceptibility of the person affected, on the other hand, may exert an important rôle. We have the two types of the disease, described as glanders and farcy; but, in addition, each of these is subdivided into an acute and a chronic form. The first signs of the disease are usually general febrile disturbance; whilst the wound, if present, shows redness, swelling, and lymphangitis. The mucous membrane of the nose may then become involved, and the nodules which are formed may break down, forming ulcers which give rise to a muco-purulent discharge. An eruption of papules may now appear on the face and on other parts of the body, and these may form vesicles, and finally pustules. This disease may run a very rapid course, or may extend over months. In the other type of the disease the lymphatics are chiefly affected, and at intervals along their course they may become enlarged and filled with purulent material, forming what are called farcy buds. In the later stages it may exhibit the nasal and other lesions; so that, as already stated, no sharp line can be drawn between the two types.

Diagnosis.—In the early stage the disease is to be recognised by the history alone, as the symptoms at that period might be ascribed to various fevers, and even pyæmia. The fact that those affected are almost invariably employed among horses, and are therefore liable from time to time to come into contact with diseased animals, or the morbid discharges from them, greatly assists in coming to a decision, as one can, as a rule, easily trace the mode of communication. Where a wound exists, the origin of the disease is, of course, obvious.

In the case of animals, where the disease frqeuently runs a very chronic course, so that the diagnosis from the signs and symptoms may be quite impossible, an absolutely decisive opinion may be formed by the injection of mallein. This consists of a glycerin extract of the culture of the glanders bacillus, which gives rise, on injection into an infected animal, to a marked rise of temperature and a distinct local swelling.

In the more chronic cases, it has been suggested that the disease may be confounded with tubercle and syphilis; but if any such doubt should exist, a bacteriological examination of the material, controlled, if necessary, by inoculation of animals, should at once settle the question.

Prognosis.—The prognosis in glanders is always unfavourable, in the acute form only 1 or 2 per cent. of those affected recovering; but, on the other hand, in the more chronic form, as many as 50 per cent. may recover. The longer the period of incubation, and the more slowly the symptoms develop, and the less pronounced the constitutional disturbance, the more hopeful is the prognosis.

Treatment.—**Local.**—Any bite or open wound which may have come in contact with suspected glanders material, should be disinfected and cauterised at once with strong carbolic acid, and if seen at a later stage, may even then be excised with advantage. The abscesses and collections of glanders material should be opened and evacuated on the ordinary surgical principles, and great care should be exercised as regards the disinfection of all the discharges.

Constitutional.—Our aim must be to support the strength of the patient, and generally to avoid the tendency towards death.

<div align="right">G. E. CARTWRIGHT WOOD.</div>

SNAKE-BITE.

DISEASE resulting from the introduction into the system of a poisonous secretion produced by certain members of the Ophidia, known as snake venom, which gives rise to acute local and constitutional symptoms.

In the British Isles the only venomous snake is the common viper (*Pelias berus*); in India, the cobra (*Naia tripudians*); in Australia, the brown snake (*Diemenia superciliosa*), the tiger snake (*Hoplocephalus curtus*), the black snake (*Pseudechis porphyriacus*), and the death adder (*Acantophis antarctica*); and in America, the rattle-snakes (*Crotalus adalanteus*), and the moccasin (*Ancistrodon piscivorus*) are the most common.

Etiology and Pathology.—The older accounts given by different observers of the action of snake venom on animals have been so contradictory, that no definite conclusions could be drawn from their results; but quite recently C. J. Martin has been able to explain these by taking into consideration the amount of the poison and its method of introduction. The active ingredients of venom appear to consist of a proteid body, coagulated and rendered practically inert on heating to 85° C., and a non-coagulable diffusible proteid which is unaffected by subjection to this temperature. He has been able to accomplish the separation of these two bodies by filtration through a film of gelatin or silicic acid, occupying the pores of the porcelain of a Pasteur-Chamberland filter. The diffusible uncoagulable proteid, which is an albumose, passes through unchanged into the filtrate, while the coagulable ingredient of the venom is retained on the surface of the filter. The coagulable proteid poison acts directly on the blood corpuscles, inducing their disintegration, giving rise to intra-vascular clotting, which is a frequent cause of death in animals when the venom is injected intravenously. It also acts as a direct poison to the cardiac muscle. When injected subcutaneously, it acts directly on the lining wall of the blood vessels and of the blood corpuscles, giving rise to effusion and hæmorrhages. This poison accordingly acts directly on the tissues, giving rise to the local symptoms and to the hæmorrhages from the blood vessels which are so frequently observed. The uncoagulable proteid or albumose, on the other hand, affects chiefly the nervous system, paralysing especially the respiratory centre in the medulla oblongata, and also the nerve terminations in muscles.

The difference in the results observed by the introduction of the venom subcutaneously or intravenously is due to the much slower absorption in the first case, of the poison, especially the non-coagulable proteid, into the circulation. When introduced directly into the blood, the experiment is usually brought to a termination by the occurrence of intravascular clotting, which masks and prevents the development of the symptoms produced by the action of the albumose poison. The proportion of coagulable to non-coagulable poison present in different venoms varies enormously, that of the rattle-snake (*Crotalus*) containing as much as 25 per cent., whilst that of the cobra contains only 1·75 per cent. (Weir Mitchell and Reichert). This fact accounts for the variation in the local and constitutional effects produced by the bites of different species of snakes.

Calmette states that the physiological action of the venoms of different species of snakes is in essence alike. The only difference consists in the local action of the venoms, and the poison which produces this effect can

be separated from those which produce the general constitutional effects due to bulbar intoxication. This is effected by heating the venom at 85° C. for fifteen minutes, when the venoms of different species (colubrine or viperine) produce similar symptoms, differing only in the inequality of their activity. Phisalix and Bertrand, and later Calmette and Fraser, have been able, by accustoming animals to gradually increasing doses of the venom, to produce an antitoxic serum which is usually termed antivenin. Calmette states that his serum produced from the cobra de capello is active against the venoms of all other serpents, and even of scorpions, so that one serum can be used in all cases of snake-bites.

Symptoms.—The local symptoms consist chiefly of pain, swelling, ecchymoses, and partial paralysis. If the patient should recover from the immediate effects, cellulitis and sloughing may ensue from the organisms which have found an entrance into the weakened tissues with the venom. The constitutional symptoms consist of general depression, nausea, fainting, accompanied by hurried respiration, loss of consciousness, and coma.

Treatment.—The immediate treatment should consist in the application of a tight ligature between the site of the bite and the heart, which may be followed by incision or destruction of the bitten part. A 5 or 10 per cent. solution of permanganate of potash, or, as recommended by Calmette, a 2 per cent. solution of hypochlorite of lime, which he states destroy the activity of the venom, may be injected locally before the ligature is removed.

The only constitutional treatment from which at present any success can be expected, is that of attempting to antagonise the action of the poison by the injection of venom antitoxine, a method which is still on its trial. The strength of the patient must of course be supported by stimulants, such as alcohol and ammonia, and artificial respiration may be resorted to for the purpose of assisting the patient over the period of acute intoxication.

<div align="right">G. E. CARTWRIGHT WOOD.</div>

GOUT.

GOUT is the manifestation of a number of morbid tendencies, some of which may be inherited and some acquired, which result in the different diseases associated with the arthritic diathesis. If the joints become affected, articular or regular gout results; if other organs or tissues become affected, then the term irregular gout is applied.

Etiology.—Gout is mainly a disease of middle and late life, but it may become manifest earlier if there is a marked hereditary tendency. It most commonly occurs among males, due, no doubt, to the habits of men being more conducive to its development than the more temperate habits of life of most women.

Hereditary predisposition is the most important factor in the determination of gout. The females of gouty families frequently escape the apparent development of gout in themselves, yet transmit the liability to the disease to their children. It is doubtful, however, whether true atavism occurs in connection with gout, that is, whether gout entirely misses a generation. It is more probable that it appears in some form,

irregular or otherwise, in the generation that it is supposed to have passed over. Excessive indulgence in alcohol, especially in the form of wines and beers, and excessive consumption of nitrogenous and rich foods, are powerful factors in the development of gout. Indolent habits and inadequate physical exercise also strongly predispose to gout. Chronic lead poisoning predisposes to gout, probably by affecting the kidneys, and so interfering with the proper elimination of uric acid.

An attack of acute gout is frequently induced by unusual indulgence in food or drink, or by some powerful emotion, such as a fit of anger, worry, or anxiety, or by exposure to cold, or by the receipt of some injury. For the production of gout, whether of the regular (articular) or irregular (abarticular) type, the deposition of sodium biurate in the organ or tissue affected is essential. The mere presence of uric acid in the blood, in the form of dissolved sodium quadriurate or biurate, is insufficient for the production of any form of gout, in the absence of deposition of the biurate from the fluids of the body.

Pathology.—Gout is associated with the presence in the blood of an excess of uric acid in combination with sodium. Uric acid—$H_2(C_5H_2N_4O_3)$ —is bibasic, and forms the following three classes of salts:—(1) the *neutral urates*, such as $Na_2(C_5H_2N_4O_3)$, the neutral sodium urate; (2) the *biurates*, such as $NaH(C_5H_2N_4O_3)$, the sodium biurate; and (3) the *quadriurates*, such as $NaH(C_5H_2N_4O_3), H_2(C_5H_2N_4O_3)$, the sodium quadriurate. Of these three classes of salts the neutral urates cannot exist in the living organism, and therefore take no part in the pathology of gout. It should also be borne in mind that uric acid does not exist in the blood in the free state. Sodium quadriurate is the soluble uric acid compound which is originally present in the blood of gouty subjects. This salt is, however, an unstable body, and after a certain time it unites with some of the sodium carbonate of the blood to form the stable but much less soluble sodium biurate. If this biurate is produced in larger quantities than the fluids of the body can retain in solution, it becomes precipitated in various structures in the crystalline form, and then constitutes the gouty deposit.

Theories of gout.—Different views have been held at various times as to the causation of gout. That which regards gout as the result of a true toxic action, exerted by the uric acid salt dissolved in the blood, is untenable for these reasons:—(1) There is no experimental proof that uric acid is a poison; (2) a gouty subject, just prior to the advent of an attack of acute gout, shows no signs of poisoning, although the fluids of his body are then saturated with a salt of uric acid; and (3) in certain blood disorders, such as severe anæmia and leucocythæmia, the blood is frequently highly charged with a salt of uric acid without the production of any toxic symptoms that could be referred to that substance. Again, the various suggestions as to the uric acid being merely a bye-product in the gouty process quite fail to explain many of the phenomena of gout. The remaining view, that the uric acid salt only exerts a baneful effect after precipitation from the blood and deposition in the tissues, appears to be the most tenable one. This theory regards the soluble uric acid salt as being destitute of poisonous qualities, and as producing no harmful results so long as it remains dissolved in the fluids of the body. When, however, the fluids become over-saturated with this compound, a crystalline deposition of sodium biurate occurs, which then acts as a mechanical irritant to the tissues and structures in which the deposition takes place.

The source of uric acid.—The over-charging of the blood in gout with

a salt of uric acid must be due to one or more of the following causes:—
(1) Production of uric acid in the normal manner, but insufficient excretion
of it; (2) over-production of uric acid while the excretion remains about
normal; and (3) diminished destruction of uric acid by imperfect oxida-
tion or by some other means. The two last-mentioned views are
untenable; for with regard to the last there is no proof that the process
of oxidation, or any other process going on within the organism, destroys
uric acid, and the second is based on the erroneous assumption that the
kidneys can only eliminate a certain amount of uric acid, whereas there is
abundant proof that an increased production of uric acid does not lead
to gout so long as the kidneys remain in a normal condition. We are
therefore restricted to the explanation of the cause of the presence of
the salt of uric acid in the blood in gout being due to the production
of uric acid at the normal seat or seats of its manufacture, and to its
subsequent imperfect excretion. That a deficient excretion of uric acid
occurs in gout, has been shown by recent accurate estimations of the
elimination of uric acid in gouty subjects.

The question next arises, whether the uric acid, which in gout is
imperfectly excreted, is manufactured in the organs and tissues of the
body generally, and thence passed into the general circulation; or whether
it is produced only in the kidneys, and then, in consequence of imperfect
excretion by these organs, the residual quantity of uric acid is absorbed
from them into the general circulation. Now, if uric acid be produced
as such in the liver, or spleen, or tissues generally, then it follows that
it must be conveyed in the blood to the kidneys in order to be excreted;
and if this be the case, it ought to be capable of detection in the blood
of healthy individuals, and of healthy animals, that excrete uric acid.
Careful examinations of the blood of healthy human beings and of various
animals has, however, always failed to reveal the presence of uric acid,
though urea is always present in such blood. This evidence suggests that
since uric acid is not conveyed in the blood to the kidneys, it must be
manufactured in those organs, and this view of the renal formation of
uric acid is supported by the fact that, although birds excrete the whole
of their urinary nitrogen in the form of uric acid, and not at all in the
form of urea, yet the blood of birds always contains an abundance of urea,
and only very minute amounts of, or no, uric acid. This evidence that the
blood of birds always contains urea, but little or no uric acid, whilst the
urinary excrement of birds contains no urea, but consists entirely of
compounds of uric acid, can only be explained by the view that the uric
acid is manufactured, at all events to some extent, in the kidneys, and that
the urea brought to the kidneys by the blood is the antecedent, or one
of the antecedents, out of which the kidneys manufacture that uric
acid.

The renal origin of gout.—It would therefore appear that the first
step in the pathogenesis of gout is a failure on the part of the kidneys
—from transient or organic mischief—to perfectly excrete the uric acid
formed in them, and that consequently absorption of the non-excreted
portion takes place from them into the general circulation, where it exists
at first as sodium quadriurate, and so forms the source from which the
gouty deposit is derived. It is probable that some affection of the kidneys
always precedes any gouty manifestations, and that this possibly transient
affection may subside if the exciting cause of it be removed, or it may
pass on to an obvious structural lesion. It may be that this renal

vulnerability constitutes the hereditary factor of gout. The affection may also be started by various causes, such as excessive indulgence in nitrogenous foods, wines, and beers, the toxic effect of lead, and the influence of nervous impulses, such as mental shocks, severe accidents, etc. The anatomical seat of the kidney affection is apparently in the epithelium of the convoluted tubes, whilst the increase of interstitial tissue is most likely a secondary change.

Uric acid is probably formed in the kidneys by the combination of urea with glycocine or with one of the derivatives of the latter body. This view is supported by the fact that uric acid can be made artificially by the union of urea with glycocine, and also by the well-known fact that amongst the carnivora, whose urine contains little or no uric acid, the bile contains no glycocholic but only taurocholic acid, and therefore yields no glycocine.

Formation and seats of gouty deposits.—As previously mentioned, the unstable sodium quadriurate circulating in the blood of gouty subjects becomes converted after a variable period of time into the much less soluble sodium biurate, which then deposits in those tissues which, either on account of having received previous slight injuries, or because of their poor vascular supply, and the sluggish movement of fluids in them, specially favour its deposition. Such tissues are structures belonging to the connective tissue class—cartilages, ligaments, tendons, and the cutaneous and subcutaneous connective tissues. It is quite possible that nervous influence may accelerate this deposition of biurate. It is well known that whatever depresses the nervous system—such as great fatigue, rage, fright, worry, or excitement—may cause an attack of gout in a gouty subject. This is probably due to nervous influences depressing the excretory power of the kidneys for uric acid, and so leading to an increased absorption of quadriurate into the general circulation. The great toe joints and the ears are the commonest seats of the gouty deposit. The reasons for the selection of the toe joints are, the liability of the joint to injury, from having to support the weight of the body, and from being subjected to sudden shocks, the remoteness of the joint from the heart, so that the force of the circulation is at its minimum at that part, and the poor vascularity of the tissues of the joint. In the helix of the ear the sluggish circulation and the coldness of the organ may account for the frequency with which uratic deposits are found in that part.

Cause of the inflammation accompanying the gouty paroxysm.—The gouty paroxysm is due to precipitation, in the crystalline form, of sodium biurate, the crystals being distributed throughout the implicated tissue in the form of delicate needles, aggregated into tufts, bundles, and stars. When deposition occurs in cartilage, the crystalline deposit acts as an irritant, and causes inflammation leading to proliferation and necrosis of cartilage cells, which may be followed by erosion of cartilage and of uratic deposits, and consequent displacement of the latter into the cavity of the joint. Although the inflammatory part of an acute gouty attack is secondary to the deposition of sodium biurate crystals, it seems to be necessary that such deposition should occur fairly copiously and suddenly, in order to start the inflammatory process. Undoubtedly, as in cases of chronic gout, the biurate may deposit slowly and quietly in joints, without the development of any acute attack.

Symptoms.—Acute gout.—Twinges of pain in some of the joints may occasionally precede the acute attack, but, as a rule, no warning

ushers in the first attack of gout. Subsequent attacks may be preceded by dyspepsia, constipation, mental depression, or loss of appetite. The seizure most frequently occurs in the early hours of the morning, when the patient is awakened by severe pain, generally in the great toe. The pain increases in intensity, but after some hours partial abatement, accompanied by a gentle perspiration, occurs. In the morning the toe is swollen, the skin is tense, shiny, of a purplish red colour, and extremely tender, and the veins are distended. During the second night the severity of the pain may recur, and such recurrence may, in the absence of suitable treatment, take place for many days. The pain in the joint is excruciating, and is quite out of proportion to the external signs of inflammation. As the attack subsides the swelling and redness of the affected part lessen, the skin itches and pits on pressure, and desquamation follows. The œdema around the joint is characteristic, and is useful in distinguishing the affection from rheumatism. Gouty inflammation of a joint is not followed by suppuration. The temperature most commonly ranges from 99° to 102° F., and the attack is generally accompanied by thirst, anorexia, and constipation, whilst the urine is scanty, high coloured, and usually deposits amorphous urates on cooling. Temporary albuminuria has been frequently observed during the early stages of a paroxysm, and occasionally slight albuminuria lasts throughout the attack. An attack of acute gout lasts on an average from eight to fourteen days in persons of strong constitution, but with advancing age the duration becomes prolonged. After an attack of acute gout a patient frequently feels much better in health than before the attack. A first attack of gout may not be followed by another, provided attention be paid to diet and the general mode of life. On the other hand, frequent recurrences may occur. The majority of first attacks of gout occur in the great toe joint, but the disease may start in the ankles, instep, knee, small hand joints, elbows, and very occasionally in the shoulders and hips. The selection of any particular joint for a primary attack is probably dependent on slight inflammatory or trophic changes in that joint, from some recent injury or strain.

Chronic gout.—As the recurrence of gout becomes more frequent, more joints are affected, and the attacks also become more prolonged, unless efficacious treatment is resorted to. Tophi are apt to form in various localities, and to give rise to the so-called *tophaceous gout.* These tophi consist mainly of deposits of sodium biurate under the skin, and are principally found in the auricles of the ears, in the vicinity of joints, and in the bursæ over joints. If excessive accumulation of the biurate occurs, these tophi assume a great size, and may then cause the integument to give way, when a discharge of a thick creamy fluid, containing an abundance of crystals of sodium biurate, takes place. The swelling in the vicinity of a joint may give rise to fluctuation, but such swelling should never be opened. Considerable enlargement and deformity of joints may occur in connection with chronic gout, to which the deposits of sodium biurate only contribute in small part. In such cases the enlargement is due to thickening of the synovial membrane, and to overgrowth of the cartilages and of the ends of the bones and surrounding fibrous tissue. This form constitutes the so-called *chronic deforming gout.* Permanent deformity of the affected joints may result, and partial dislocations and ankyloses may also occur. On the other hand, the uratic deposits may undergo complete solution, and the joint be left in an apparently normal condition. The urine of chronic gout is somewhat increased in quantity,

and is of lower specific gravity and somewhat paler than normal. The amount of uric acid eliminated is diminished. A trace of albumin is frequently present, and permanent albuminuria is a fairly common occurrence in confirmed gout. Before an attack of gout the output of uric acid is low, and is also diminished in the early part of the attack. The excretion of phosphoric acid in the urine is stated to correspond very closely to that of uric acid, being low before and during the early part of the paroxysm, but rising as the attack passes off. Oxaluria is of fairly common occurrence in connection with gouty attacks. Changes in the heart and circulation, consequent on gouty affections of the kidneys, are indicated by hypertrophy of the left ventricle, a strong cardiac impulse, displacement of the apex beat to the left, and accentuation of the aortic second sound. The pulse is of high tension, and the arteries are hard, tortuous, and sometimes atheromatous. Under such conditions a cerebral hæmorrhage may occur. Attacks of true angina pectoris, associated with arterial degeneration and softening of the walls of the heart, occasionally occur in gouty subjects.

Saturnine or lead gout.—Chronic lead poisoning gives rise to both chronic kidney disease and gout. The liability of those suffering from chronic plumbism to be attacked with gout, is probably due to the action of lead salts on the kidney epithelium causing a diminution in the excretion of uric acid, so that an absorption of the non-excreted portion takes place from the kidneys into the general circulation. The patient suffering from saturnine gout, unlike the majority of sufferers from inherited gout, is pale, thin, and anæmic. If the lead poisoning has been of short duration, the lesions may yield to treatment, but after a prolonged absorption of lead into the system the kidney condition is generally incurable.

Irregular gout.—Gout appearing in a situation other than a joint is regarded as irregular or abarticular. Irregular gout may accompany arthritic gout, or may take its place, or may alternate with it, but more frequently it occurs among those who have never suffered from gout in the joints, but who are predisposed to gout either by inheritance or by mode of life. The most important points to attend to in the diagnosis of irregular gout are the question of heredity, the habits of the patient, the nature of the attack, a careful examination of the urine, and, if possible, of the blood or blood serum; and, lastly, the successful reaction to therapeutic remedies. Probably all forms of irregular gout are due to the precipitation in the crystalline form of sodium biurate in the organ or tissue affected. Irregular gout may affect—the alimentary tract, causing pharyngitis, œsophagismus, dyspepsia, or gastro-intestinal catarrh; the air passages and lungs, causing laryngitis, tracheitis, bronchitis, or asthma; the heart and vessels, causing cardiac irritability, anginal attacks, or phlebitis; the nervous system, causing migraine, neuralgia, neuritis, or mental depression; the genito-urinary system, causing gouty kidney, or uric acid gravel, or urethritis; the skin, causing eczema, herpes, pruritus, or urticaria; and the eye, causing gouty inflammation of any of the structures of the eye, —conjunctivitis and iritis are the two commonest eye affections caused by the gouty condition. Irregular gout may also manifest itself as glycosuria or diabetes.

Retrocedent or metastatic gout.—This form of gout occurs when a sudden subsidence of the inflammation in a gouty joint is succeeded by the development of the disease in one or more of the internal organs, such as the stomach, intestines, heart, or liver. Such attacks frequently follow an

exposure to cold while suffering from an articular attack, and especially after indiscretion in diet. If the attacks rapidly shift their position, the affection is termed *flying gout.* Attacks of retrocedent gout have not uncommonly followed the baneful practice of suddenly plunging a gouty foot into cold water. It is quite possible that the attacks are caused by a deposition of the crystalline sodium biurate in the affected viscus, and that this crystalline biurate acts as a mechanical irritant, and so produces inflammation of the organ. On the other hand, the attacks may simply be of nervous reflex origin, due to vasomotor disturbance producing a condition of hyperæmia or congestion of the affected viscus. The following are the principal forms of retrocedent gout, with the symptoms indicative of the sudden transference of the attack to the affected viscus:—

Stomach.—The symptoms usually consist of severe pain in the stomach, accompanied generally by vomiting and a feeling of general oppression, depression, and faintness. Palpitation may occur.

Intestines.—The usual symptoms are severe abdominal pain, vomiting, tympanites, and constipation.

Heart.—The symptoms are severe palpitation, pain in the region of the heart, a sensation of constriction of the chest, dyspnœa, a small, feeble pulse, and great anxiety. Syncopal attacks may occur.

Brain.—Apoplexy is the most frequent symptom. Congestion of the brain or meninges may occur, and may be followed by headache, stupor, convulsions, delirium, and occasionally by maniacal attacks. Transient attacks of aphasia, amnesia, and hemiplegia sometimes occur, and are probably due to congestion of the brain.

Diagnosis.—The well-marked symptoms attending an attack of acute gout render the diagnosis easy. The subacute and chronic forms of gout may be confounded with rheumatism, rheumatoid arthritis, or with synovitis of traumatic, pyæmic, or gonorrhœal origin. The appearance of the joint, the discovery of tophi, and the family history are the main points on which to rely. The blood may also be examined for uric acid by the following method, known as Garrod's thread test:—About 2 drms. of the serum furnished by the blood, on standing, or of the fluid raised by a blister, are placed in a large watch-glass, acidulated with acetic acid to set free the uric acid, and an ultimate fibre from a piece of linen cloth immersed in the fluid; the watch-glass is then covered over and left in a warm room. When, by evaporation, the serum has been brought to the consistence of a thin jelly, the fibre, still on the watch-glass, is examined under a low power of the microscope, when, if obtained from a gouty subject, it will be found to be studded with crystals of uric acid. The important subject of the differential diagnosis of gout, rheumatism, and rheumatoid arthritis is dealt with under the last-mentioned head.

Prognosis.—If no complications arise, if the attacks are not too frequent, and if no serious amount of albuminuria occurs, the disease is not likely to materially shorten life, especially if the patient is amenable to proper treatment and discipline. The prognosis, in cases of irregular gout affecting the heart, and in cases of retrocedent gout, is much graver.

Treatment.—No routine treatment can be adopted which is suitable to all cases. The treatment of individual cases must be regulated according to the nutritional condition of the patient, his habits, surroundings, and mode of life.

General management.—It should have for its aim the following objects:—The treatment of the gouty paroxysm, and the relief of the

pain as speedily as possible; the treatment of the subacute or chronic condition, and the prevention of the recurrence of an attack, which may be effected by the promotion of the elimination of uric acid, by checking any excessive formation of uric acid that occurs in some subjects, and by careful attention to diet and general hygiene; and the treatment of the affected joint or joints, with the object of removing the uratic deposits, and of preventing permanent deformity. A careful examination of the urine should always be made, and it is especially important to ascertain whether the kidney affection is in the transient or organic stage. The indications that the gouty affection of the kidneys is passing from the transient into the organic condition are the existence of a certain amount of polyuria, a low specific gravity of urine—usually from 1007 to 1016— the presence of a small quantity of albumin and of a few granular casts, if a careful microscopical examination is made after centrifuging the urine, and a diminished daily excretion of uric acid and generally of urea. It is desirable before commencing treatment, and from time to time during treatment, to ascertain the amount of uric acid that is being daily eliminated in proportion to the body-weight of the patient. This determination must be made on a sample of the mixed urines of twenty-four hours, as the mere determination of the percentage of uric acid in a casual sample of urine constitutes no guide to the actual amount that is being daily excreted.

Treatment of acute gout.—*Local.*—If the gouty paroxysm occurs, as it most frequently does, in a great toe joint or foot, the limb should be slightly elevated above the level of the body, and a cradle arranged to take the weight of the bedclothes off the affected part. To alleviate the severe pain, a pack of cotton-wool should be arranged round the affected joint, and should be saturated with a warm lotion containing sodium carbonate, belladonna liniment, and laudanum. The pack should be changed every eight or twelve hours. No attempt at local depletion—such as the application of leeches to the inflamed joint, blistering, or incisions—should on any account be made. Nor should cold bathing or cold application to the joint be attempted. For the internal treatment of acute gout, colchicum is a most valuable drug. It should be especially used for acute gout, and for subacute attacks supervening on chronic gout, as, if used continuously, tolerance is apt to be acquired, and then the drug ceases to act. At the commencement a large dose of 30 to 40 minims of colchicum wine should be given, followed by a mixture containing in each dose 10 to 20 minims of the wine, with from 40 to 60 grs. of citrate of potassium, which should be taken three times a day. The citrate of potassium is given for its combined properties of acting as a diuretic and of diminishing the acidity of the urine. Colchicum reduces the gouty inflammation, relieves the pain, and shortens the attack. It is a powerful direct cholagogue, and it is probably owing to its action on the liver, by inhibiting the formation of glycocine, and so diminishing the formation of uric acid in the kidneys, that the efficacy of colchicum in mitigating the severity of the pain and relieving an attack of gout is due. From 3 to 4 grs. of blue pill should be given the first night, and should be followed by a dose of Epsom salts in the morning. In the employment of purgatives for gouty patients the great object is not to produce powerful purgation, but to relieve portal congestion. A very useful pill is one containing either 2 grs. of euonymin or ¼ gr. of podophyllin, combined with 1 gr. of extract of hyoscyamus and 1½ gr. of the compound extract of colocynth. If the pain of an acute attack of gout is so severe as to prevent sleep, 10 grs. of chloral,

sulphonal, trional, or phenacetin may be given, or a dose of 1 gr. of extract of hyoscyamus, given with blue pill at night, will in some cases act as a very useful anodyne. It is doubtful whether salicylates are of any use in the treatment of true gout.

Dietetic—For the first day or two of an acute attack the patient should be restricted to a milk diet, which may consist of milk, arrowroot and milk, bread and milk, milk puddings made with rice, sago, or tapioca, and tea made with boiling milk instead of with water. Weak tea, with cold toast thinly buttered, may also be taken. The free drinking of hot or cold water, or of some mineral water free from sodium salts, should be encouraged. During the acute stage no alcohol should be given, unless there are strong reasons for its administration, such as a weak action of the heart, and a feeble, irregular pulse, when a little well-matured whisky, diluted with an aerated water, will prove the best form of alcohol. Beef-tea, and any of the meat extracts or essences, should be avoided at all times by gouty patients, owing to the tendency they have to irritate the kidneys, and so to interfere with the elimination of uric acid. With the subsidence of the acute attack, the patient may return to a more liberal diet.

Treatment of chronic gout.—The excessive formation of uric acid may be checked by careful attention to diet and regimen, by the promotion of the metabolism of the liver, and by the relief of congestion of the portal system. In addition to colchicum, which may be given in small doses, guaiacum may be very usefully administered as an alterative, which stimulates the metabolism of the liver, and also affords relief to the portal system. From 5 to 10 grs. of guaiacum resin should be given in cachets two or three times a day. If constipation occur, a sulphur and guaiacum tablet, or a dose of compound liquorice powder, should be taken at night. An occasional dose of blue pill and euonymin, followed by a purge of Epsom salts, will be found useful. The elimination of uric acid may be promoted by encouraging free diuresis, by the drinking of sufficient quantities of water, and by the administration of citrate of potassium, which increases the volume of the urine, and at the same time diminishes its acidity. The use of the citrate of potassium may with advantage be pushed until moderate alkalinity of the urine is produced. A patient suffering from gout should avoid, as far as possible, the use of common salt at table, on account of the power that it possesses of hastening the precipitation of sodium biurate.

To reduce the chronic inflammatory thickening of the fibrous tissues around gouty joints, iodide of potassium may be given in doses of 5 to 10 grs. three times a day, and may usefully be combined with from 5 to 10 minims of tincture of iodine. Careful massage and gentle exercise of the stiffened joints should be employed, but only when convalescence is fairly established; massage and muscular movements increase the flow of lymph in the lymph channels, and so tend to promote the removal of uratic deposits, and to increase general metabolism. If the œdema around a joint should persist, the hot douche, followed by sponging with a cold, strong solution of common salt, will be found serviceable. The thermal baths of Bath, Buxton, Aix-les-Bains, as well as other spas, and mud baths, are useful in the treatment of cases of chronic articular gout. The lithium salts, which have for some time had a reputation of being solvents of gouty deposits, probably do not possess any such power, but since they are powerful diuretics, they may, on that account, be of some use in the treatment of

chronic gout. They should never, however, be given in sufficient quantities to keep the urine alkaline, as their depressing effect in such doses is too great. After convalescence, as much exercise as possible, short of fatigue and discomfort, should be taken in the open air. Cycling is an excellent exercise for the gouty, since it furnishes good muscular movement in the open air, without the gouty joints having to bear the weight of the body.

Treatment of retrocedent gout.—If the symptoms are urgent, some brandy should be given, and if necessary, morphine injected hypodermically, provided marked albuminuria does not exist. If the metastatic seizure affects either the heart or brain, it may be desirable to reinduce an attack of articular gout by placing the feet in a hot mustard and water bath. For the treatment of the cardiac form, heart tonics and brandy should be administered, and a mustard leaf applied to the epigastrium. If an anginal attack occurs, then, in addition, a dose of nitroglycerin should be given at once, or an inhalation of nitrite of amyl employed. For the treatment of the cerebral form, if the patient is plethoric, if the pulse is hard, and stupor or coma supervene, venesection should be performed, and from 8 to 16 oz. of blood withdrawn; in less urgent cases, six leeches may be applied to the mastoid region. For the treatment of the gastro-intestinal form of retrocedent gout, a mustard leaf should be applied to the epigastrium, and a mixture containing bismuth subcarbonate, sodium bicarbonate, and hydrocyanic acid should be given.

Treatment of irregular gout.—One form of irregular gout, the gouty heart, is associated with fatty degeneration of the cardiac walls, and is generally evidenced by vertigo, faintness, palpitation, irregular pulse, insomnia, and slight anginal attacks. The treatment should be rest in the recumbent position; and a small dose of blue pill or calomel, followed by a purge of Epsom salts, should be administered. A mixture containing convallaria and strychnine may be given, and if anginal attacks occur, nitroglycerin or erythrol tetranitrate may be given by the mouth, or inhalations of nitrite of amyl employed. The patient must be carefully dieted; and graduated exercise, at first of a passive nature, such as massage, and later of an active kind, such as resistance exercises, may be very beneficial. For the treatment of gouty phlebitis, which is a fairly common form of irregular gout, the patient should be kept in the recumbent position, and any sudden movement of the affected limb must be prevented, on account of the danger of detaching a portion of the thrombus, and the occurrence of consequent embolism of the pulmonary artery. Equal parts of glycerin and extract of belladonna should be smeared over the affected part, and a linseed poultice, with some of the glycerin and belladonna spread on the surface, should be applied and renewed every six hours. In addition, the ordinary treatment of the gouty state must be resorted to. For the treatment of gouty sciatica, the patient must be kept in the recumbent position, and in severe cases the pain should be relieved by a hypodermic injection of morphine. Ammonium chloride, in doses of 30 to 40 grs. three times a day, is a very useful drug in the treatment of this complaint. Two grs. of hydrobromide of quinine should also be given in a pill, two or three times a day, and, in addition, the ordinary treatment of the gouty state will probably have to be resorted to.

Treatment of gouty glycosuria and gouty diabetes.—Dietetic treatment should be resorted to, without, however, restricting the diet too much. An excessively nitrogenous diet is to be avoided as tending to accentuate the gouty condition, but no hard-and-fast rules as to the amount

of diet can be laid down. Each case must be treated by ascertaining what amount of proteids, fats, and carbohydrates are best borne by the individual. Toasted bread, milk, and milk puddings made with rice, sago, and tapioca, are generally permissible in this form of glycosuria. The best test of the suitability of the diet is the fact that the weight of the patient is not diminishing, while at the same time the excretion of sugar is becoming less. A pill, containing 1 gr. of blue pill, 1 gr. of acetic extract of colchicum, and 2 grs. of euonymin, should be given every other night; and a mixture containing 30 grs. of ammonium chloride and 15 minims of dilute nitro-hydrochloric acid should be taken three times a day. The mineral waters best suited for the treatment of gouty glycosuria and diabetes are those of Carlsbad, Kissingen, Leamington, Llandrindod, Marienbad, Neuenahr, and Vichy.

Preventive treatment of gout.—Whatever promotes the elimination of uric acid, and so prevents its absorption into the general circulation, tends to prevent the occurrence of gout. This can be effected by—the promotion of increased diuresis; the production, at all events intermittently, of a moderate degree of alkalinity of the urine; and by stimulation of the metabolism of the liver, and of the kidney cells engaged in the excretion of uric acid. The first effect can be secured by the patient drinking a sufficient quantity of ordinary water, or of a suitable mineral water; the second object is attained by the consumption of sufficient quantities of vegetable food, and by the occasional administration of citrate of potassium; and the third, by the administration of suitable cholagogues, such as guaiacum, and an occasional euonymin and blue pill. Careful attention should be given to diet. Regular habits and sufficient exercise should be encouraged, and constipation should be avoided.

Diet in gout.—A rational mixed diet is the one best suited for gouty patients. The assumption that a purely vegetable diet is the best for the gouty is erroneous, since it makes no difference as regards the production of uric acid, whether the proteid matter be of animal or vegetable origin ; but since animal tissues are so much richer in proteids than a vegetable diet, the amount of the former taken by the gouty should be strictly limited. Due consideration should always be given to a patient's experience of what articles of diet disagree and agree with him. It is important that a gouty patient should take a sufficiency of water to drink, so that the various organs are well flushed, the removal of the gouty deposits encouraged, and the specific gravity of the urine kept moderately low. The quantities of fluids taken in the twenty-four hours should not be less than 3½ pints, and may even with advantage reach to 4½ pints. It is an excellent custom for a gouty person to slowly sip half a pint to a pint of hot water in the morning immediately after rising, and at night before retiring to bed ; if desired, the water may be flavoured with a slice of lemon peel.

For breakfast, a selection may be made from the following articles of diet:—Porridge and milk, whiting, sole, plaice, fat bacon, and eggs cooked in various ways. Dry toast thinly buttered, and tea infused for three minutes, should be taken with breakfast. At lunch and dinner, no soup should be taken. The varieties of fish most suitable to the gouty are whiting, sole, turbot, and plaice. Meat should be taken at only one meal, and then in moderate quantity. Beef, mutton, chicken, turkey, pheasant, and calf's sweetbread are admissible. Salted meat, salted and smoked fish, shell-fish, and articles of food pickled in vinegar,

should be avoided. Two vegetables should be taken at both lunch and dinner, and in abundant quantities. The vegetables that should be avoided by the gouty are asparagus, tomatoes, and green peas. Any of the other ordinary vegetables may be taken, of which the most useful are spinach, Brussels sprouts, French beans, cabbage, turnip-tops, turnips, and celery. Stewed or baked fruits may with advantage be taken every day at one meal, and a milk pudding at the other meal. Rich pastry and all rich sweets should be avoided.

As regards the employment of alcohol, if the gouty person be of robust habit of body, total abstinence is best. If, however, the cardiac action be weak and failing, moderate quantities of alcohol should certainly be allowed. In cases of chronic gout, a moderate amount of alcohol may be necessary for the promotion of digestion. A tablespoonful of matured whisky, freely diluted, constitutes the best form of alcohol. Of wines, light but sound clarets, Moselles, and hocks are least open to objection. Port, burgundy, champagne, ale, and stout should be avoided by the gouty.

Mineral waters in the treatment of gout.—The value of a given mineral water in the treatment of gout depends greatly on the main object with which it is taken—whether to remove gouty deposits, or to stimulate the action of a sluggish liver and to relieve portal congestion, or for the treatment of gouty dyspepsia, or to relieve the bowels in cases of torpor and gastro-intestinal catarrh, or to act on the kidneys, or to relieve gouty affections of the skin. The use of a mineral water, so far as its employment with the object of removing gouty deposits is concerned, lies solely in its watery constituent, and does not in any way depend on the mineral constituents dissolved in it. For such a purpose, the springs which contain no sodium salts, or traces only, are the ones suitable for such cases; these are the simple waters classified in the first group. In cases of sluggish action of the liver, of gastro-intestinal catarrh and torpor, of gouty dyspepsia, and of other forms of irregular gout, mineral waters containing sodium salts are beneficial, owing to the action of these salts as hepatic and gastro-intestinal stimulants. The various mineral waters used in the treatment of gout may be classified into the six following groups :—

The simple waters, or waters comparatively free from sodium salts.— These are the waters that are especially useful for the removal of uratic deposits in the joints and tissues. The principal waters of this class are those of Buxton, Bath, Strathpeffer, Contrexéville, Aix-les-Bains, Pfaffers, Gastein, Wildbad, and Vittel.

The simple alkaline waters.—These contain sodium bicarbonate, and are useful for the treatment of hepatic congestion, dyspepsia, and gastro-intestinal catarrh. The principal waters of this class are those of Vichy, Vals, Neuenahr, Salzbrunn, and Fachingen.

The alkaline sulphated waters.—These contain sodium bicarbonate and sulphate, and generally a moderate proportion of sodium chloride, and are useful for the treatment of the same class of disorders as mentioned in the previous group. The principal waters of this class are those of Carlsbad, Marienbad, Tarasp-Schuls, Cheltenham, and Leamington.

The alkaline muriated waters.—These contain sodium bicarbonate and chloride, and are useful for the treatment of gouty dyspepsia, and of gouty catarrhal affections of the respiratory organs. The principal waters of this class are those of Ems, Royat, Assmannshausen, and La Bourboule.

The muriated waters.—These contain sodium chloride as their principal constituent, and are useful for the treatment of gastro-intestinal and

hepatic gout, and gouty dyspepsia. The principal waters of this class are those of Homburg, Wiesbaden, Kissingen, Baden-Baden, Nauheim, Llandrindod, Woodhall Spa, and Llangammarch Wells.

The sulphur waters.—These contain sulphur, either in the form of sulphuretted hydrogen only, or, in addition, some of the sulphur may exist in the form of the sulphides of calcium, magnesium, and sodium. They are useful in the treatment of gouty skin affections. The principal waters of this class are those of Harrogate, Strathpeffer, Aix-les-Bains, Aix-la-Chapelle, Baden, Llandrindod, and Weilbach.

<div align="right">A. P. LUFF.</div>

ACUTE RHEUMATISM, OR RHEUMATIC FEVER.

AN acute systemic disease, probably dependent upon an unknown infective agent, and characterised by arthritic and cardiac manifestations, as well as a tendency to inflammation of other fibrous tissues.

Etiology.—Acute rheumatism is essentially a disease of adolescence and of early adult life, although no period of life, except early infancy, is exempt. In early life, up to the ages of 18 or 20, and especially among children, the disease is somewhat more common in females; but, taking all ages together, males are affected oftener, owing, no doubt, to the occupations of men involving a greater tendency to the disease, from exposure to cold and wet.

That there is some hereditary transmission of a liability to this disease is generally believed. Cheadle considers that the tendency to rheumatism is transmitted as strongly as the tendency to gout. Whilst admitting the probability of some inherited tendency to rheumatism, the writer's experience is that it is not nearly so great as in cases of gout. Chill is the most important factor in determining an attack of acute rheumatism. The chill may result from exposure to cold, or from a wetting, or from a sudden change of temperature. Those occupations involving exposure to cold and to great changes of temperature, are predisposing causes to rheumatic fever. One attack of acute rheumatism does not afford immunity from a future attack; on the contrary, the individual is predisposed by one attack to subsequent attacks. Acute rheumtism is more frequent in temperate, subtropical, and humid climates. In this country it is most prevalent in the autumn. According to Newsholme, it prevails most in dry years, when the subsoil water is abnormally low, and the temperature of the earth is high.

Pathology.—The view that is rapidly gaining ground is, that the symptoms of acute rheumatism are due to an infective organism, and to its elaborated toxine or toxines. This view is supported by the fact that there is a marked resemblance between the entire course of rheumatic fever and that of an infective disease, as seen in the character of the fever, the involvement of the joints, the liability to endocarditis and pericarditis, the sweats, the anæmia, and the tendency to relapse. The proof that is wanting that the disease is infective in its nature, is the association of a specific micro-organism with the complaint. Achalme has described a bacillus, similar in appearance to that of anthrax, which he found in the heart blood and in the cerebro-spinal fluid of two cases of acute rheumatism, which were examined soon after death; he also found

the same bacillus in the blood of living cases. Whether this is the specific organism of rheumatic fever, is doubtful. Poynton and Paine have recently discovered a diplococcus which is present in the blood and tissues of patients suffering from acute rheumatism, and which causes symptoms resembling rheumatic fever, with endocarditis, in animals. Newsholme considers that the general evidence is in favour of a microbic *materies morbi*, which he thinks is essentially a soil organism. In support of his view, he refers to the occasional concentration of the disease in epidemic form in certain cities, or in streets, and even in certain houses, and also to many of the clinical features of the disease being in favour of its infective nature, namely, the mode of onset with aching, the shivering in many cases, the sore throat, the progress of the fever, its complications, and its tendency to relapse. He thinks that the channel of infection is the tonsils or some part of the naso-pharynx, for tonsillitis is very common among cases of rheumatic fever, and that the well-known influence of injury, fatigue, and chill is to lessen the resistance of the individual. The frequency with which rheumatic fever occurs in particular houses tends to support the infective theory of the disease, and Lees even considers that the disease is probably a house disease, and that its prevalence would be diminished if every house had an impermeable basement. Newsholme inclines to the opinion that a low level of ground water is an indication of certain conditions of dryness and temperature of the subsoil favourable to the growth of the telluric contagium of acute rheumatism, which view is supported by the fact that the disease is most common in the autumn, reaching its maximum in October. In support of the theory that acute rheumatism is an infective disease, Newsholme has shown that the rate both of the mortality and of the frequency of the disease fluctuate in a manner very similar to those of such infectious diseases as scarlet fever and erysipelas.

Two theories as to the causation of acute rheumatism, which are now practically abandoned, are the chemical theory and the nervous theory. The *chemical theory* assumed that acute rheumatism was due to the production, within the system, of lactic or uric acids. The lactic acid theory probably owed its origin to the well-known sour smell and acid reaction of the sweat, and the diminished alkalinity of the blood, which always accompany acute rheumatism. It was assumed that, owing to defective metabolism, lactic acid or some combinations of lactic acid are produced, and constitute the *materies morbi*. There is no evidence whatever in support of this view. As regards uric acid being the causative factor of acute rheumatism, it is not likely that that substance could be the cause of such diverse pathological conditions as those met with in gout and rheumatism. The *nervous theory* regards the nerve centres as being primarily affected, and regards the joint and other troubles as being of a trophic character. As opposed to this view, no lesion of the nervous system is associated with acute rheumatism.

Morbid anatomy.—The pathological process in the affected joints consists of hyperæmia, and swelling of the synovial membranes and fibrous tissues, with exudation of a small amount of fluid into the cavity of the joint. The fluid is turbid, albuminous, and contains some leucocytes and a few fibrin flakes. A purulent effusion is very rare. Occasionally there may be slight erosion of cartilages. The fluid in the joints is usually absorbed in a few days, and acute rheumatism rarely causes permanent injury of a joint. Lees and Poynton have shown that acute rheumatism may affect the heart muscle apart from valvular affection, a condition

which is probably due to the poison of the disease producing a direct effect upon the cardiac muscle; and Sansom has pointed out that valvular disease may arise secondarily as a sequela of changes which were originally myocardial. The striking feature in the cardiac muscle fibres is the extreme fatty change. In cases of hyperpyrexia, the blood usually contains an excessive amount of fibrin.

Symptoms.—Acute rheumatism.—The onset of acute rheumatism may be abrupt, but in most cases is gradual, and is frequently preceded by slight malaise, by tonsillitis (according to Fowler, sore throat occurs in about 80 per cent. of the cases), and by irregular pains in the limbs and joints. The temperature rises quickly, and within twenty-four hours from the onset, the disease, as a rule, is fully developed. The temperature ranges from 100° to 104° F., and is very irregular, with marked falls and rises, being highest in the evening. The pulse is rapid and soft. The tongue is moist, covered with a white fur, and is often thickly coated. There is loss of appetite, great thirst, and constipation. Pain usually begins in one of the larger joints—knee, hip, elbow, shoulder, or ankle—and soon becomes extremely severe. The urine is scanty, high coloured, and very acid. Profuse acid sweats occur over the entire body, and the sweat, in the majority of cases, possesses a peculiar sour odour, which is probably due to fermentative changes after secretion. Sudamina are very frequently present in abundance, especially over the chest and abdomen. Except in cases of hyperpyrexia, the mind remains clear, and no delirium occurs. The joints are swollen, hot, and reddish, and are excessively painful to move. They are attacked successively, and the joints usually attacked are the knees, ankles, elbows, wrists, shoulders, and hips. One of the characteristic features of the disease is the migratory nature of the joint affection; a joint which one day is swollen and painful may the next day be free from swelling and pain, as the inflammation tends to subside in one joint, and to develop in another. The amount of joint swelling is variable, but it is rare to find extensive effusion, and much of the enlargement that occurs is not due to effusion into the cavity of the joint, but to infiltration of the peri-articular tissues with serum. When the wrists and ankles are affected, it is common for the tendon sheath to be involved in the swelling, by which means the enlargements of the hands and feet are considerably added to. Amongst the most distressing of the symptoms of the disease are the agonising pains in the joints, causing sleeplessness, the drenching sweats, and the extreme prostration. The duration of the fever is variable. In young adults, if no complications arise, the acute symptoms frequently subside in eight or nine days, and convalescence is established in another ten days. Relapses, however, are of very common occurrence. The defervescence of temperature is usually gradual, and the remissions are frequently found to be coincident with the sweats. The effect of treatment with salicylates is generally to reduce the temperature to the normal in from four to five days, or less.

Anæmia is a fairly prominent symptom of rheumatic fever; it develops rapidly, and is associated with some leucocytosis. The urine, as a rule, is reduced in amount owing to excessive loss of water by sweating, is of high specific gravity, 1020–1030, and possesses a high colour. It has a very acid reaction, and is clear when first passed, but on cooling it deposits an abundant quantity of amorphous urates, and occasionally some crystals of uric acid. The chlorides of the urine are generally diminished in amount, or may be absent altogether. Febrile albuminuria not un-

frequently occurs. The heightened colour of the urine is due to the presence of a large quantity of hæmatoporphyrin, and of a small quantity of urobilin. The saliva may become acid, and is said to contain an excess of sulphocyanides.

On account of the great liability of the heart to be affected during an attack of rheumatic fever, it should be examined each day that the patient is under observation; and attention should also be directed from time to time to the lungs. The advent of pericarditis, endocarditis, pleurisy, or pneumonia is generally marked by a rise of temperature.

Subacute rheumatism.—This is a milder form of the disease with less pronounced symptoms. The temperature rarely rises above 101° F.; fewer joints are involved, and the arthritis is less intense.

Acute rheumatism of childhood.—In children the non-arthritic manifestations of rheumatism are especially frequent and prominent, while the articular manifestations are either slight, or may be absent altogether. These points must be carefully borne in mind, as otherwise a wrong diagnosis may be made, and irreparable harm inflicted on a child by consequent erroneous treatment and insufficient rest. In early life the joint tissues seem to be much less susceptible to rheumatic inflammation, whilst the non-arthritic manifestations, which are so prominent at that period, are the formation of subcutaneous fibrous nodules, erythema, purpura rheumatica, chorea, endocarditis, and pericarditis. In childhood the disease is most common in girls, and, according to Cheadle, in 70 per cent. of the cases among children there is a definite family history of rheumatism. The profuse acid perspirations, so marked in adults, are not common in children. Inflammation of the endocardial covering of the valves is nearly twice as common among children as among adults, and it is especially liable to come on insidiously in children. It is therefore extremely important to diagnose minor attacks of rheumatism in children, as they are frequently attended by a subacute endocarditis or pericarditis. In connection with this point, it should be borne in mind that the so-called "growing pains," of which children so frequently complain, are, in the great majority of cases, rheumatic pains. Parents ought to be impressed with the fact that physiological growth is never accompanied by pain, and that these erroneously called "growing pains" are pathological in their origin, and frequently require treatment, as otherwise the child may lapse into the rheumatic condition.

Acute rheumatism does not occur in early infancy. Cheadle states that he has never met with the disease at that period of life, a period when infantile scurvy and syphilitic affections of the ends of the long bones especially occur, and which are apt to be mistaken for acute rheumatism.

Complications and sequelæ.—The complications and sequelæ of acute rheumatism are important and serious. It is a question whether the heart affections which so frequently occur in connection with acute rheumatism should be considered as complications, or rather as part of the disease. It is convenient, however, to include and consider them in this category. The complications and sequelæ of acute rheumatism may be arranged in seven groups, namely, cardiac affections, hyperpyrexia, rheumatic nodules, pulmonary affections, cerebral complications, cutaneous affections, and anæmia.

Cardiac affections.—These consist of endocarditis, pericarditis, and myocarditis. Endocarditis is the most frequent and serious complication of acute rheumatism. It occurs in perhaps over 50 per cent. of cases, and,

according to Church, it affects the sexes equally. The liability to endo-
carditis increases directly with the number of attacks, rising, according to
Mackenzie, from about 58 per cent. in first attacks to about 70 per cent.
in third attacks; but, on the other hand, the liability to the complication
diminishes as age advances. The mitral segments are most frequently
affected, and the inflammatory changes in the valves lead to sclerosis and
retraction of the segments, and so to chronic valvular disease. Ulcerative
endocarditis is of very rare occurrence in the course of acute rheumatism.
Pericarditis may occur independently of, or together with, endocarditis.
It is much more frequently met with in acute rheumatism than as a
complication of any other disease. According to Church, it occurs more
frequently among men than women, and generally begins at a much later
period in the attack than endocarditis does. The risk of pericarditis is
much greater in first attacks than in subsequent ones. A peculiar form of
delirium not uncommonly develops during the progress of rheumatic
pericarditis. Myocarditis is most frequently noticed in connection with
combined endocarditis and pericarditis, and Church considers it probable
that in all but the slightest cases of pericarditis a certain amount of
myocarditis is present. It is quite possible that slight degrees of
myocarditis occur more frequently in the course of acute rheumatism than
is generally suspected. The anatomical condition is a granular or fatty
degeneration of the cardiac muscle, which leads to weakening of the walls
and to dilatation.

Hyperpyrexia.—This is a very serious complication. The temperature
may rise rapidly a few days after the commencement of the attack of acute
rheumatism, and, with the rise of temperature, the pain in the joints
lessens, the profuse sweating diminishes, and the patient becomes at first
extremely restless; later on, the hyperpyrexia may be associated, though
not necessarily, with delirium. This complication is more common in
first attacks of acute rheumatism, and especially occurs during the second
week of the attack. The temperature rises from 105° to 111° F. The
pulse is feeble and frequent, the patient becomes extremely prostrated, and
if death is about to occur, a condition of stupor comes on, passing into coma.

Rheumatic nodules.—These consist of small subcutaneous fibrous
nodules attached to the tendons and fasciæ. They vary in size from a
small shot to a large pea, and are most numerous on the fingers, hands,
and wrists, but also occur about the elbows, knees, spines of the vertebræ,
and the scapulæ. In children they are most commonly found upon the
backs of the elbows, over the malleoli, and at the margins of the patellæ.
As a rule, they are not tender. They frequently develop with great
rapidity, and usually last for weeks or months. They are more common
in children than adults, and are particularly associated with severe
endocarditis. Cheadle considers that the eruption of large nodules
signifies persistent and uncontrollable cardiac disease, which almost
invariably terminates fatally. Histologically, the nodules present a
structure similar to, if not identical with, that found in the nodular
growths on the cardiac valves.

Pulmonary affections.—Pneumonia and pleurisy are occasional com-
plications of acute rheumatism, especially in connection with endocarditis
and pericarditis. Congestion of the lungs occasionally occurs.

Cerebral complications.—Chorea is apt to develop in connection with
slight attacks in childhood. Delirium is usually associated with hyper-
pyrexia, but also may be excited by the over-administration of sodium

salicylate, or the employment of the drug in an impure state; it is generally of the active and noisy kind, but frequently, in cases of hyperpyrexia, passes into the low, muttering variety, followed by stupor and coma. Coma, which is a serious symptom, may occasionally develop without preliminary delirium, and sometimes independently of hyper-pyrexia. Convulsions only occur on rare occasions, but they may precede the advent of coma. Meningitis is an extremely rare complication.

Cutaneous affections.—As previously mentioned, sudamina are extremely common in acute rheumatism. A red miliary rash may develop, and scarlatiniform eruptions very occasionally occur. Purpura, urticaria, and various forms of erythema are not uncommonly met with.

Anæmia.—This is rather a constant accompaniment of rheumatic fever than a complication. Hayem and Garrod have shown that a considerable fall in the number of red corpuscles and some slight leucocytosis accompany an attack of acute rheumatism.

Diagnosis and prognosis.—The differential diagnosis of rheu-matism, gout, and rheumatoid arthritis is dealt with in a subsequent article (see pp. 485–487). In addition to gout and rheumatoid arthritis, pyæmia, secondary to bone disease, may be mistaken for acute rheumatism. The occurrence of rigors, the detection of bone disease, the non-migratory nature of the joint affections, and the absence of profuse sweats, tend to distinguish pyæmia from acute rheumatism.

The course of acute rheumatism is extremely variable. The mortality during an acute attack is very small, and is then nearly always due to hyperpyrexia, or to some secondary lesion, such as pericarditis or endocarditis, or, more rarely, pneumonia or pleurisy. Sudden death in rheumatic fever, though a very exceptional occurrence, is most frequently due to myocarditis; more rarely it results from embolism. The prognosis in acute rheumatism is far more serious in the case of children than in that of adults, mainly owing to the greater liability among children to endocarditis and pericarditis.

Treatment.—A patient suffering from acute rheumatism should wear a woollen night-gown, which should be frequently changed if much sweating occurs. The bed should be flat and smooth, and the patient should lie on blankets, and be lightly covered with blankets only. No sheets should be used, on account of the liability to chill when they become soaked with perspiration. Absolute and prolonged rest is a most essential factor in the treatment of acute rheumatism. The diet during the acute stage should consist mainly of milk, to which some common salt may be added with advantage. Ewart recommends the addition of 15 grs. of salt to each half-pint of milk. In addition, good soups, especially made with vegetables, and animal broths in moderate quantities, may be given. Lemonade, barley water, infusion of tamarinds, or imperial drink, should be freely given to allay the thirst. As convalescence is established, the patient may be put on a fuller and more liberal diet.

With regard to drug treatment, there are two methods which are specially employed, one is the treatment with salicyl compounds, and the other the alkaline treatment. Maclagan considers that the salicyl com-pounds exert a specific and curative action on the disease. Certainly, if administered in sufficient quantities, they rapidly relieve the pain and reduce the temperature. The alkaline treatment, which was first advocated by Fuller, was based on the theory that rheumatism was due to the presence of an acid in the blood. It is the opinion of many observers that

heart complications are less frequent among those patients who have been treated with alkalies, and this has been ascribed to the influence of the alkalies in preventing the coagulation of fibrin. In the experience of the writer, acute rheumatism is most successfully treated by a combination of a salicyl compound with an alkali. For an adult, 20 grs. of sodium salicylate and 30 grs. of potassium bicarbonate should be given every two hours, until the pain is relieved and the patient is fully under the influence of the salicylate, when the same quantities should be given every four hours till the temperature has fallen to normal. Afterwards, 15 grs. of salicylate and 20 grs. of the bicarbonate should be given every four hours for about a fortnight. If the salicylate is pushed too far, it produces deafness, noises in the ears and head, and delirium, which are indications for the reduction in the dose, or even possibly for its withdrawal. These effects are to a great extent obviated by producing a free action of the bowels at the outset by means of a dose of calomel, followed by a saline purge, such as magnesium sulphate or sodium sulphate. Moreover, the sodium salt of the natural salicylic acid should be employed, as the artificially prepared salicylic acid is much more liable to produce toxic effects, probably on account of the presence of paracresotic acid in it. If by any chance the sodium salicylate is not well tolerated, an equal quantity of salicin should be substituted for it, and given in combination with the bicarbonate. Maclagan prefers the use of salicin as not being a depressant to the nervous system, and advocates the use of 20 to 30 grs. every hour till the fever and acute symptoms disappear. The heart should be carefully examined each day during the administration of the salicylate and alkali, as they tend to exert a depressing effect on it. If pericarditis or endocarditis supervenes, it is advisable to discontinue the use of the salicylate, and to substitute salicin for it. Sodium salicylate should not be given in the acute rheumatism of children. For children, salicin and alkalies should be employed. For the relief of the pain in the joints, tincture of iodine may be painted over each affected joint, which should then be completely enveloped in a hot linseed poultice, and surrounded with plenty of cotton-wool and a flannel bandage; the entire dressing should then be left untouched for twenty-four hours. Another method of considerably relieving the pain and inflammation of the joints is by the application of salicylate of methyl. A piece of lint saturated with about a teaspoonful of salicylate of methyl is placed over the affected joint, and upon this a piece of guttapercha tissue, overlapping the lint by about an inch all round, is laid; the edges of the under portion of the guttapercha tissue are then sealed down to the skin by wetting with a little chloroform, after which some wool and a bandage are applied. At the end of twenty-four hours the salicylate of methyl will be found to have undergone complete absorption. The only drawback to this method of treatment is the peculiar penetrating odour of the salicylate of methyl. The pain in the joints may also be relieved by the application of chloroform liniment, or by applying blisters above and below the joints, or by the light application of the Paquelin thermo-cautery.

For the general relief of pain, it is occasionally advisable to administer opium in the form of Dover's powder, and phenacetin, antifebrin, and antipyrine are sometimes useful for the same purpose, but these drugs exercise no beneficial action on the disease. If cardiac failure and prostration occur, moderate quantities of brandy (2 to 3 oz. in the twenty-four hours) may be given, but in cases complicated with severe endocarditis, peri-

carditis, or myocarditis, stimulants must be given more freely. For the prevention of cardiac complications, Caton applies small blisters (about the size of a florin) between the clavicle and the nipple, over the first, second, third, and fourth dorsal nerves, either on the right or the left side. They are applied one at a time, and repeated at different points. These nerves are possibly in close association with the heart, and the treatment, which is strongly advocated by Caton, is very successful. During convalescence the cinchona preparations or quinine should be given. Iron is frequently not well borne, but it should be cautiously tried on account of the anæmia. It is best administered in the form of the scale compounds or of Blaud's pills. Patients should be kept in bed for about six weeks, in order to prevent the liability to relapses and to cardiac complications.

Hyperpyrexia requires prompt and energetic treatment. It is best treated by immersion of the patient in a cold bath at a temperature of 65° F.; and as the temperature of the water is raised by the immersion of the patient, ice should be added. If facilities for the cold bath are not at hand, then the ice-pack, or the rubbing of the body with lumps of ice, will prove very effective. In either case, the head should be sponged with ice-cold water, or an ice-bag should be applied. If possible, the patient should be kept in the bath till the temperature has fallen 6°, but if shivering occurs the patient must be removed at once from the bath or pack. The bath may have to be repeated several times, and stimulants should be given to combat any collapse. Endocarditis and pericarditis must be suitably treated, as described in connection with those diseases.

A. P. LUFF.

CHRONIC RHEUMATISM.

MANY cases supposed to be chronic rheumatism are cases of chronic rheumatoid arthritis or of chronic articular gout. Most frequently the affection takes the form of slight recurrent articular attacks, especially in those with a family history of rheumatism. The articular attacks may come on insidiously, and especially occur in persons past middle life. Another class of cases, those of chronic abarticular rheumatism, are most frequently met with in children, and in early adult life. These cases consist of such rheumatic manifestations as subcutaneous fibrous nodules, erythema, and chorea, which have been previously referred to. A chronic form of rheumatism affecting the finger-joints is that known as *rhumatisme fibreux*, in which the finger-joints present fusiform enlargements, due to thickening of the joint capsules.

Morbid anatomy.—The synovial membranes are injected, but usually there is not much effusion into the cavities of the joints. Interference with the movements of the joints results from thickening of the capsules, ligaments, and tendon sheaths in the neighbourhood of the joints, and from a certain degree of atrophy of the muscles.

Symptoms.—There is stiffness of the affected joints, and pain, which varies with changes in the weather, and which is more marked after rest. The joints are tender and a little swollen, and the joint affection usually shows the same tendency to shift from joint to joint as in the acute disease. Creaking in the affected joints is very common, and ankylosis may occur

in those cases which are sequels of acute rheumatism. The temperature is seldom raised.

Prognosis and treatment.—Chronic rheumatism is obstinate as regards treatment, and the affection, when once settled in a joint, may persist indefinitely, but does not necessarily shorten life. Attacks of articular pain usually yield rapidly to treatment with sodium salicylate, but in the more chronic cases the salicyl preparations may be useless. Iodide of potassium and guaiacum are sometimes very beneficial; the iodide should be given in doses of 5 to 15 grs. in a mixture, and the guaiacum resin in doses of 5 to 10 grs. in cachets. Quinine and alkalies are also frequently useful. Local treatment, in the form of counter-irritation and massage, is often of great benefit. Useful adjuncts in the treatment of chronic rheumatism are radiant heat baths, superheated air baths, electric baths, brine baths as at Droitwich, peat baths as at Strathpeffer, hot alkaline baths, and douche massage. Cold and damp weather should be avoided.

MUSCULAR RHEUMATISM.

This is a term applied to a myalgia resulting from exposure to cold and damp, or from muscular overstrain. Probably the affection has no direct relationship to acute rheumatism. Various views have been advanced to explain the causation of the muscular pain, such as active hyperæmia, or a neuralgic affection of the terminations of the nerves in muscles, or slight inflammatory changes in the fibrous tissues of the muscles.

Etiology.—Muscular rheumatism is most commonly met with in men, particularly among those exposed to cold, and to sudden alterations of temperature. Persons of a rheumatic or gouty habit are especially prone to the affection.

Symptoms.—Pain, especially when the affected muscles are used or put upon the stretch, is the most prominent symptom, while tenderness on pressure of the affected muscles is also an important diagnostic sign; the affected muscles are frequently spasmodically contracted, as in cases of stiff neck or rheumatic torticollis, in which the sterno-mastoid is the seat of the affection. In very acute cases, especially in cases of the variety known as "lumbago," the pain comes on with extreme suddenness, frequently giving the impression that a muscle has been over-strained, but in chronic cases the onset is gradual and insidious. In acute cases the pain usually lasts only a few days, but in chronic cases it may persist for months or longer.

The forms of muscular rheumatism may be classified according to the groups of muscles involved. These are—

Lumbago.—This form is almost entirely met with in adult life. It affects the muscles of the loins and their tendinous attachments. The pain is greatly increased by movement, and especially by stooping and then resuming the erect posture. The patient may be quite unable to turn in bed, or to rise from the sitting position.

Intercostal rheumatism, or pleurodynia.—This affection of the intercostal muscles is diagnosed by the absence of the signs of pleurisy and of herpes zoster, and by the pain elicited on pressure over the affected muscles. A deep breath or coughing also causes intense pain.

Rheumatic torticollis, or stiff neck.—This form especially occurs in

childhood. One or both sterno-mastoids may be affected, but usually the attack is confined to one side. The affection is accompanied by muscular spasm, and the patient in attempting to turn the head rotates the whole body.

Treatment.—Rest of the affected muscles is most important; in cases of intercostal rheumatism, strapping the side gives great relief by insuring the necessary rest. Sodium salicylate is most useful for the relief of the pain, especially in acute cases, and it may be usefully combined with full doses of nux vomica. In chronic cases, alkalies, in conjunction with potassium iodide and guaiacum resin in cachets, should be given. In very acute cases it may be necessary to give a local subcutaneous injection of morphine for the relief of the pain. For acute cases of lumbago, acupuncture is very effective; needles of about 4 in. in length are thrust into the affected muscles, and withdrawn after five to ten minutes. A very useful method of treating many forms of muscular rheumatism is to have an embrocation, consisting of equal parts of the compound camphor liniment and of soap liniment, well rubbed over the affected area, and then to have the part ironed with a hot iron through a sheet of brown paper spread over the skin, the iron being as hot as can be borne by the patient. Muscular rheumatism is also successfully treated by radiant heat baths, superheated air baths, electric baths, ordinary hot baths, brine baths, and peat baths.

<div align="right">A. P. LUFF.</div>

RHEUMATOID ARTHRITIS.

THIS is a progressive degeneration of the joints, consisting of changes in the synovial membranes, cartilages, and bones, accompanied by atrophy of some structures and by hypertrophy of others. In chronic cases, marked osteophytic outgrowths are peculiar to this disease. Rheumatoid arthritis, which is a distinct disease from gout and rheumatism, has frequently been mistaken for one or other of these diseases, and the confusion has doubtless been intensified by the ambiguity of the terms used to describe the disease. Rheumatoid arthritis is known under the various names of " osteo-arthritis," " rheumatic gout," " arthritis deformans," "polyarthritis deformans," chronic rheumatic arthritis," " pernicious arthritis," and *"rhumatisme chronique infectieux."* In Germany and America it is generally known as "arthritis deformans." Heberden was one of the first to distinguish between this disease and rheumatism. He pointed out that there was swelling of the affected joint, but little or no fever, no great pain, and no redness of the skin; that the disease generally attacked joint after joint, and that it was very crippling; that the fingers and wrists were especially liable to the disease, and that the terminal phalangeal joints of the fingers were liable to become affected with nodosities, which have since become known as " Heberden's nodes."

Etiology.—Rheumatoid arthritis, in its rarer and acute form, occurs especially in children and young adults, whereas in its commoner and chronic form it is most frequently seen at and after middle life. In its chronic form it is much more common amongst women than men, probably on account of the liability of women to affections of the genito-urinary tract, to excessive child-bearing, and from prolonged lactation. Direct inheritance of rheumatoid arthritis cannot be clearly traced, as in the

cases of gout and rheumatism, but in those inheriting a tendency to joint troubles one member of a family may develop gout, another rheumatism, and another rheumatoid arthritis. Rheumatoid arthritis almost entirely occurs in debilitated subjects, and is therefore a frequent sequela of any condition which has impaired the nutritional state of the body generally. Injury to a joint, using the term injury in its widest sense, such as that caused by rheumatism, gout, gonorrhœa, septic troubles, etc., predisposes to this disease. Rheumatoid arthritis is common amongst the poor and ill-nourished. For its successful treatment an abundant and generous diet is required. Cold and damp soils and sudden alterations of temperature are favourable to the development of the disease.

Morbid anatomy.—The disease of the joints involves cartilage, bone, and synovial membrane. The synovial membrane is usually the first part of the joint to become affected. The articular ends of the bones become thickened, and present projecting osteophytic growths. The inflammatory process causes denudation of the cartilage, which ultimately leads to exposure of the surface of the bone. The exposed surfaces of the bones then become eburnated by mutual friction, the eburnated portions being hard and polished. The synovial membrane is generally thickened, and the amount of synovial fluid is increased. The capsules of the joints become thickened, and may be the seat of ossification. In the early stages of the disease the spindle-shaped swellings of the affected joints are mainly due to thickening of the synovial membranes, and of the capsules of the joints, and only to a very slight degree to osteophytic outgrowths. The nodular protuberances, so suggestive of the disease in its later stages, are in part due to ossification of the hypertrophied cartilages at the periphery, and in part to osteophytic outgrowths from the bone. These osteophytic outgrowths may lead to complete locking of the joints. The ligaments of the joints are usually considerably thickened, and so assist in the locking of the joints. The heads of the bones may undergo either hypertrophy or atrophy. No deposits of sodium biurate occur in the joints as in gout, and the disease differs from chronic rheumatism in the existence of extensive structural alterations. Bursal swellings are occasionally met with in the vicinity of the affected joints. The fingers are frequently deflected to the ulnar side, a deformity which is probably due to disease of the metacarpo-phalangeal joints, and the toes may show a similar deflection. Spasm of the atrophied muscles may cause various deformities, such as flexion of the limbs at the knees, elbows, and wrists, and flexion of the metacarpo-phalangeal joints, with hyper-extension of the first interphalangeal and compensatory flexion of the terminal phalangeal joints.

Pathology.—At the present time two views are held by different observers as to the origin of rheumatoid arthritis. One view attributes it to a nervous cause, while the other regards it as an infective disease due to micro-organisms settling in the joints. Those who favour the nervous view argue that the changes in the joints are similar to those met with in the chronic spinal arthropathies, such as are met with in locomotor ataxy, syringomyelia, and hemiplegia, and that the muscular atrophy and the dystrophies of the nails and skin that are frequently associated with rheumatoid arthritis are of neurotic origin. Moreover, it is stated that the symmetrical progress of the disease which is so often seen, and the occasional indications of neuritis during life, and of its very occasional discovery post-mortem, support the view as to the nervous origin of the disease. Senator regarded the facts that the muscular wasting may be out

of proportion to the joint mischief, and that the disease may be started by violent emotion and grief, as evidences of the origin of the disease from a central nervous cause. On the other hand, those who favour the view that rheumatoid arthritis is an infective disease, find support in the facts—(1) that it frequently occurs as a sequela to some acute infection, such as acute rheumatism, influenza, gonorrhœa, scarlet fever, and tonsillitis; (2) that its acute mode of onset in certain cases is suggestive of an acute infective process; (3) that the rheumatoid arthritis of children is associated with widespread enlargement of lymphatic glands and swelling of the spleen; and (4) that in a certain number of cases, micro-organisms have been discovered in the fluid of the joints. Bannatyne and Wohlmann have isolated a short, dumb-bell-shaped bacillus from the synovial fluid, synovial membranes, cartilages, and the bony débris of erosions of affected joints in cases of rheumatoid arthritis. In a few instances they have also isolated the same bacillus from the blood. The organism was not found in the fluid of the joints in other cases of synovitis. The observations of Bannatyne and Wohlmann have been confirmed by Blaxall. Recently, von Dungern and Schneider made cultivations of the organism from a case of rheumatoid arthritis, which after many years ended fatally, and on injecting cultures into the joints of rabbits they state that a similar articular disease was produced to that from which the patient had suffered.

With regard to these two views, it is, in the first place, probable that under the name of rheumatoid arthritis more than one distinct disease is included, and it is possible that the acute and chronic forms may be distinct diseases, and due to entirely different causes. The balance of evidence seems to be in favour of acute rheumatoid arthritis being an infective disease, and that it is due to a settlement of micro-organisms in the affected joints, that there they produce a toxine, and that that toxine, passing into the circulation, is responsible for any nervous symptoms which occur in the disease. Certainly the tachycardia, local sweatings, and pigmentation which frequently accompany rheumatoid arthritis, are readily explicable if absorption of certain toxines into the general circulation occurs, without requiring the agency of the nervous system to account for them.

The usually symmetrical nature of the affection first gave support to the view that the disease was nervous in its origin, but, as opposed to this, it must be borne in mind that it does not begin in a symmetrical way. It generally begins in one joint on one side, and then spreads. Another reason for supposing the disease to be of nervous origin is on account of the muscular atrophy which takes place when the larger joints are affected. This muscular wasting, however, goes on in every form of chronic arthritis in which there is much disuse of muscles. If this wasting were due to any central nervous affection, there would be present in the affected muscles the reaction of degeneration, which, however, is never obtainable in rheumatoid arthritis. Perhaps the most serious objection to the nervous hypothesis is, that no central nerve lesion has ever been discovered. Careful examinations have been made of the spinal cord in cases of rheumatoid arthritis, but no lesions or degenerations have been found.

Symptoms.—The disease occurs in acute, subacute, and chronic forms. The acute and subacute forms are characterised by inflammatory changes in the affected joints, by erosion of cartilages and bones, by nerve and trophic phenomena, and by glandular enlargement. It is polyarticular, and in its acute and subacute forms occurs especially in children and young adults. The disease usually commences in one joint, commonly one of the

metacarpo-phalangeal articulations, and then rapidly spreads to most of the other joints. The symmetrical nature of the affection is usually well marked, and the joints are painful, hot, and present a spindle-shaped enlargement, but no outgrowth or thickening of either cartilage or bone. The chronic forms are characterised by progressive thickening and hardening of all the joint structures, by the formation of osteophytes, by the lipping of cartilages, and by the development of deformities. The disease in its chronic form may be the later stages of an acute attack, or may be chronic from the outset. It may affect several joints, or be confined to one or two.

As a rule, rheumatoid arthritis commences insidiously. It usually begins with pain, not necessarily severe, in the affected joint or joints, which is especially apt to occur after an exposure to chill, or after some depressing condition. Pain in the ball of the thumb is very suggestive of the commencement of rheumatoid arthritis. The swelling of the joint is slow, and grating on rubbing the ends of the bones against each other is only obtained later in the course of the disease.

The three divisions of the disease proposed by Charcot constitute the best classification of the forms of rheumatoid arthritis for a study of their symptoms. They are—cases with Heberden's nodes, the general progressive form, and the partial or monarticular form.

Cases with Heberden's nodes.—These cases represent the mildest degree of the disease. The nodes consist of little hard swellings of the finger joints, especially of the terminal phalanges, and are due to a very chronic form of rheumatoid arthritis. This type is more commonly met with in women than in men, and usually at or after the middle period of life. The nodules are due to enlargement of the ends of the bones, which are frequently covered by a pouch of the projecting synovial membrane, which acts somewhat as a bursa. The joints become swollen and tender, the cartilages are softened, and the ends of the bones are eburnated. After a time the disease usually becomes arrested, but the swellings remain, and eventually may cause no discomfort. Osler states that the subjects of these nodules rarely suffer in the larger joints.

The general progressive form.—Of this there are two varieties—the acute and chronic. The acute form has been previously referred to. It may resemble, and certainly has been mistaken for, acute articular rheumatism. It generally starts in one joint, and subsequently involves many. There is not much redness of the affected joints, and only moderate fever. It is most common in children, young adults, and young women. Among the last-mentioned it is often connected with recent delivery, rapid child-bearing, or excessive lactation. The chronic form is much commoner than the acute. The joints that have been most especially and actively used, according to the former occupation or employment of the patient, are those which usually show the first signs of the disease. The affection commences with slight swelling and pain on movement. The amount of effusion into the joint is variable, and may be marked or slight. The hands and feet, especially the hands, are most liable to be first affected, and the disease then tends to advance more or less up the limbs towards the trunk, obeying, as Charcot described, "the centripetal law." In extreme cases every joint in the body may be affected. The temporo-maxillary articulation becomes the seat of rheumatoid arthritis in about 25 per cent. of the total number of cases. At a later period the articulations of the spine may become involved. The disease usually

attacks the cervical vertebræ first, causing pain at the back of the neck, and rendering fixation of the neck and rotation of the head difficult. The dorsal and lumbar vertebræ may be next affected, so that in bad cases the spine may be converted into a rigid column. Pain may be very severe, especially at night, while, on the other hand, the case may proceed to extreme deformity without pain.

Very considerable alteration in the shape of the joints may occur from the formation of osteophytes, thickening of the capsules, and retraction of muscles. The cartilages become worn away at the centres, and the ends of the bones become eburnated by attrition and chronic osteitis. In such joints grating is readily obtained by rubbing the eburnated ends of the bones against each other. The locking of the joints, which sometimes ultimately occurs, is not due to true ankylosis, but to the presence of the projecting osteophytes, and to the thickening of the capsules of the joints. True ankylosis only occurs in the spinal column in cases of rheumatoid arthritis. Atrophy of the muscles from disease is present in bad cases, with contractures tending to flex the thigh or to bend the knee or elbow. Most patients finally reach a stage in which the disease becomes arrested, so that they are free from pain, and only are troubled with the associated crippling and consequent inconvenience. Increased rapidity of the heart's action is a not uncommon accompaniment of the disease in its earlier stages, and cold and moist hands and feet are commonly met with. Subcutaneous fibroid nodules and periosteal nodes are occasionally met with, especially in those cases which are secondary to rheumatism, and a rheumatoid pigmentation of the skin, somewhat resembling freckles in appearance, is not unfrequently seen. In a small proportion of cases a neuritis is present, but it probably is always secondary to the arthritis, and may be caused, as suggested by Bannatyne, either by the existing joint inflammatory process, or by the action of toxines circulating in the blood. Spender describes the following collateral symptoms, one or more of which are commonly present, as aids to diagnosis in doubtful cases:—Tachycardia; pigmentation of the face, and perhaps numerous spots or stains on the arms; cold and moist hands; neuralgic twinges in the upper and lower limbs; persistent neuralgic pain over the ball of the thumb, and on the ulnar side of the wrist.

The partial or monarticular form.—This form is met with especially in old persons, and is more common amongst men. It is most frequently seen in the knee, hip, shoulder, and spinal column. In the hip it is the disease known as *morbus coxæ senilis,* and in the spine it is known as *spondylitis deformans.* The cases of the monarticular form are especially apt to follow an injury of some kind.

Arthritis deformans in children.—Still describes a variety in which general enlargement of the joints is associated with swelling of the lymphatic glands and of the spleen. It occurs nearly always before the second dentition, and more frequently in girls. It generally commences in an insidious manner, with slight stiffness in one or two joints, and then others gradually become involved; but the onset may occasionally be more acute, and be attended with fever. The enlargement of the joints is due more to general thickening of the soft tissues than to enlargement of the ends of the bones. There is no grating to be obtained in the joints.

Diagnosis.—The differential diagnosis of gout, rheumatism, and rheumatoid arthritis is a matter of importance, when it is borne in mind that the treatment of these three diseases is quite different. Cases are

frequently diagnosed as cases of chronic rheumatism in which there exist great deformities—lipping of the cartilages, osteophytic outgrowths, and grating of the ends of the bones. These are cases of rheumatoid arthritis. In chronic rheumatism, neither lipping of the cartilages nor the osteophytic outgrowths, which are so diagnostic of rheumatoid arthritis, ever occur.

A rough clinical test in the diagnosis of a chronic articular affection, but one which is frequently of assistance, is to ascertain the effect of treatment with salicylate of soda. If the case responds well to this treatment, it is most probably a case of rheumatism. If it does not respond to this treatment, the existence of rheumatoid arthritis or gout is fairly certain, as neither of these affections responds well to salicylates. It is highly probable that the oft-heard remark about "an obstinate case of rheumatism which has not done well with salicylates" is due to the case being one of gout or of rheumatoid arthritis—more probably the latter.

Rheumatism in its subacute or chronic forms, and especially in the form known as *rhumatisme fibreux*, certainly may affect the joints, but it never produces that gross permanent deformity which the other affections may, such, especially, as the lipping of the cartilages and the bony outgrowths already referred to. In the condition of *rhumatisme fibreux*, fusiform enlargement of the small joints may occur, due to thickening of the joint capsules, but there is an absence of lipping of the cartilages and of osteophytic outgrowths. The actual diagnosis of rheumatism is usually a fairly easy matter. If a patient complains of pains in the joints, which pain flies about from joint to joint, and generally affects some of the muscles at the same time, and if, in connection with these flying pains, there are indications of the presence of the rheumatic erythema—erythema nodosum—then the diagnosis of rheumatism is obvious. As a rule, the fitful way in which the joints are affected, the fairly rapid subsidence of the swellings of the joints, and the association of muscular pains, make the diagnosis a simple matter. Then the response of the disease to treatment by salicylates will settle the diagnosis.

As to the distinction between rheumatoid arthritis and gout, a mistake is more likely to be made, but it should be avoided if some patient observation be given to the case. The unfortunate name of "rheumatic gout," as applied to rheumatoid arthritis, is no doubt a cause of gout and rheumatoid arthritis being confused. The following distinguishing characters show how very different are the two diseases. Rheumatoid arthritis occurs most commonly in females, gout occurs mostly in males. Rheumatoid arthritis occurs most commonly amongst the poor and ill-nourished, and especially under conditions of depressed health, prolonged anxiety, and exposure to damp and sudden alterations of temperature; gout mostly among the well-to-do and well-nourished. Rheumatoid arthritis is a disease which is improved by good dieting; in the case of a gouty person a spare and plain diet is indicated. The onset of rheumatoid arthritis is insidious; that of gout sudden and obvious. As regards the commencement of the attack, gout most commonly begins in one of the feet, especially in the great toe joint; rheumatoid arthritis, although ultimately it frequently affects many joints of both hands, nearly always begins in one joint, most commonly selecting one of the joints of the thumb, either the carpo-metacarpal or metacarpo-phalangeal joint, after which it rapidly spreads to the other joints. In the joint affections of rheumatoid arthritis there is no obvious swelling at first, and no marked redness; in the joint affections of gout,

at the commencement of acute or subacute cases, there is very obvious swelling, marked redness, and a shiny condition of the skin around the affected joint. In rheumatoid arthritis there is very little pain at first. There is some aching in the joint, but the affection starts in a very insidious manner. It is this insidious character of the disease which is one of its bad features, for the patients do not seek advice until the affection is fairly advanced. Gout, however, begins in the most marked manner with severe pain, the patient, as a rule, waking up in the early morning with excruciating pain in the great toe. Therefore, if doubt exists as to whether a particular case be one of rheumatoid arthritis or of gout, the patient should be questioned as to the commencement of the attack, in order to ascertain whether it began with an obvious outburst of pain, and with swelling and redness of the joint, or whether it began very insidiously. The particular joints affected in the two diseases assist somewhat in the differential diagnosis. Then as to the joint affections, in addition to the general statement that gout generally begins in the foot, and rheumatoid arthritis generally in the hand, an important factor in the differential diagnosis of the two diseases is, that there is a joint commonly affected in rheumatoid arthritis which is not affected in cases of gout, namely, the temporo-maxillary articulation. The writer has never seen a case of gout in which the temporo-maxillary joint has been affected, whereas in rheumatoid arthritis it is extremely common for that joint to be involved. Another distinction is this, and it is perhaps one of the most important, namely, that in connection with rheumatoid arthritis there is a remarkable symmetry in the affection of the smaller joints of the hands. In gout that symmetry is wanting. It was this symmetrical affection of the joints which led to the idea that rheumatoid arthritis is a nervous disease. Lastly, in a case of simple rheumatoid arthritis, sodium biurate is not found in the joints or tissues, whereas in the gouty person sodium biurate exists in the affected joints and frequently in other tissues.

It is not common to have rheumatoid arthritis and gout associated in the same patient. What occasionally does occur is, that gouty deposits may form in joints suffering from rheumatoid arthritis, but it is more in the nature of an accident than anything else. A person suffering from rheumatoid arthritis who indulges in rich living for a lengthened period of time, and especially if he takes too much wine, may develop gout, and gouty deposits in the joints of a patient suffering from rheumatoid arthritis may occasionally be met with. Still, it is only a complication; there is no actual relationship between the two conditions, and one in all probability does not predispose to the other. Rheumatism certainly predisposes to rheumatoid arthritis, because a person who has been subject to rheumatism has the nutrition of the joints so much impaired for the time, that if there is any opportunity for the specific micro-organisms to gain access to those joints, it is very likely that they will there develop and flourish. That is probably the reason why rheumatoid arthritis is not uncommonly met with in persons who have previously suffered from rheumatism.

Prognosis.—In the early stages the disease is curable, if prompt and efficient treatment is employed. In the later stages the prognosis is not so good, as almost the best that can then be expected is to arrest the disease and so prevent further damage to the joints.

Treatment.—Rheumatoid arthritis, if left untreated, tends to spread from joint to joint, and produces progressive destruction of the joint tissues. Occasionally treatment fails to effect any arrest of the disease,

and this is especially apt to occur in connection with the rheumatoid arthritis of the old. As previously stated, the disease is curable in the early stages, but in chronic cases the best that can be expected of treatment is that the progress of the disease shall be stopped, and that a fair amount of improvement or restoration of the joints shall occur. It is doubtful if any treatment can effect complete repair of the disorganised tissues. For the successful treatment of this disease, it is essential that the treatment should be commenced while the disease is in its early stages; hence the importance of an early recognition of the malady, and of its distinction from gout and rheumatism. The treatment must be persevered in over a lengthened period of time, probably a year or two, and during the treatment everything possible must be done to increase the patient's strength. The not infrequent mistake of diagnosing rheumatoid arthritis as gout, and the consequent placing of the patient on a restricted and spare diet, has undoubtedly led to the development of severe and incurable forms of the disease. The diet should be as liberal and as good as the patient can digest, and animal food should be partaken of freely, though not to the exclusion of vegetables. A moderate quantity of wine or stout should be taken with lunch and dinner. Woollen clothing should always be worn next the skin; and exercise, short of producing pain, should be indulged in. A dry gravel soil and a warm, dry climate are most suitable to patients suffering from this disease.

The treatment of rheumatoid arthritis by drugs must be quite different from that of gout or rheumatism. Efficient measures must be taken to improve the general condition and health of the patient. Cod-liver oil and maltine should be given after meals. The iron preparations in combination with arsenic are also useful. Garrod strongly recommends the employment of iodide of iron. In addition to these, the two drugs that have proved to the writer most effectual in the treatment of the disease are carbonate of guaiacol and methylene-blue. Of these the carbonate of guaiacol appears to be the more efficient remedy. It is a white crystalline powder, which is slowly decomposed in the intestinal tract, the liberated guaiacol being absorbed into the blood. If the disease is due to the elaborated poisons of micro-organisms, then it is possible that the guaiacol may destroy or render inert those toxines. The carbonate of guaiacol should be given in cachets, or as a powder, in doses gradually increased from 5 to 10 grs., three times a day. Methylene-blue should be given in 2-gr. tabloids, at first twice a day, and afterwards three times a day. A patient taking methylene-blue should be warned that the urine and fæces will be stained an intense blue colour, but the writer has never found harm to arise from the administration of the drug. After the administration of methylene-blue for some time, the conjunctival membrane is temporarily stained a very pale blue colour, but no discoloration of the skin occurs.

The thermal treatment of the affected joints, either by means of baths, superheated air, or radiant heat, is most beneficial. Douche massage is the most effective form of treatment with hot water, and perhaps next to that ranks the peat bath, such as can be obtained at Strathpeffer. Radiant heat baths, in which the affected joints are bathed in the heat and light rays reflected from a number of incandescent electric lamps, are also beneficial in many cases. Electric baths, using the alternating current either from an alternating dynamo supply or from an induction coil, are also most useful in the early stages of rheumatoid arthritis.

Properly regulated movements and properly applied massage are of great use in overcoming the stiffening and fixation of the joints, and the muscular wasting in their vicinity. Massage, in addition to its local influence upon the affected joints and their proximate muscles, also improves the general circulation and the general nutrition of the body. General massage should therefore be lightly applied at first, little or no attention being paid to massage of the affected joints for the first few days. The form of manipulation which may be applied to the joints with the best results is *massage à friction*, which consists of the application of quick frictions or rubbings to the surfaces of the joints. In addition, gentle kneading and squeezing of the parts, particularly of the tendons and fibrous surroundings, should be effected. The effects of such manipulations are generally evidenced by the rapid absorption of exudative products in and around the joints. Active and passive movements of the affected joints should also be employed.

If possible, a patient suffering from rheumatoid arthritis should not winter in this country. A dry, warm atmosphere is required, which can be best obtained in Egypt and Algeria.

If the locking of a joint is extreme, and is otherwise incurable, it may be advisable to excise the joint. Successful excisions of the elbow and knee in cases of rheumatoid arthritis have been performed.

<div align="right">A. P. LUFF.</div>

RICKETS.

RICKETS is a disease of infancy and early childhood, usually commencing during the second half of the first or in the second year of life; it is a disease of nutrition, and while its most characteristic feature consists in the enlargement of the epiphyses and other deformities of the bones, the muscles, ligaments, and various internal organs are usually affected.

Etiology.—In considering the origin of rickets, the following facts are worthy of remark. Rickets is a rare disease among the peasants of southern Italy and in other warm climates, where it is the universal custom for mothers to suckle their infants for the first year, and on account of the favourable climatic conditions, the infant is able to spend the greater part of the day in the open air. Rickets is a very common disease in Lancashire and other manufacturing districts in this country, where large numbers of infants are artificially fed either wholly or in part, and are exposed to the unfavourable conditions of a cold and damp climate, and spend a great part of their time in the unwholesome air of crowded dwellings. From a consideration of these facts, and others that might be cited, it is tolerably certain that the chief factors in producing rickets are exposure to cold and damp, breathing unwholesome and vitiated air in dwelling-houses, and taking food which in quality and quantity is not suitable for the delicate digestion and assimilative powers of the infant. On the other hand, it is clear that the powerful factors in preventing rickets are abundance of fresh air and sunlight, well warmed and ventilated dwelling-houses, and breast-feeding for the greater part of the first year of life.

It is important to note that, while Italian infants do not suffer from rickets when born and reared in their native country, they are apt to suffer more or less severely when born and bred in large cities and in

colder countries than their own, even though they are suckled by their mothers. This is true of Italian infants in New York (Holt), and also in this country. Negro infants appear also to suffer far more severely than the white American children in cities like New York and Boston. Presumably the infants belonging to the southern races are more sensitive to the influence of cold and damp, than the infants of those who are natives of the country. Doubtless the negro population and the Italian working-class population are among the poorest and worst housed classes in the northern American cities. It must be borne in mind that in this country infants who are nursed by a healthy mother for the first eight or nine months of life mostly escape becoming rickety, yet a minor degree of rickets is not uncommonly seen in infants who are breast-fed, especially in those in whom lactation has been prolonged for upwards of a year. Breast-fed infants share the same insanitary conditions as artificially fed infants, as far as exposure to cold and the bad air of dwelling-houses are concerned, and indeed often suffer more from exposure, as, being dependent on their mothers for their food, they are taken about wherever the mother goes. From the evidence before us it is clear that rickets is certain to be a common disease among the lower classes of a manufacturing district, crowded together in courts and slums; where the mothers from necessity or choice are unable to suckle their infants, and give them a mother's care; where the infant is badly clothed, carelessly fed, and exposed to all the various bad influences which ignorance and carelessness produce. Rickets will be a rare disease where the mother is strong and healthy, able both to suckle the infant and devote her time to its care and nurture; where the climatic conditions are favourable, and the infant is given fresh air and protected from the effects of cold and damp.

We may briefly summarise the chief causes of rickets as :—

1. Dietetic.—The infant, during the first six or nine months, has been improperly fed, or, as the result of chronic dyspepsia, has been unable to digest and assimilate its food. Very probably, as the result of indigestion, certain deleterious substances, perhaps toxines, have been formed in the alimentary canal and absorbed into the blood.

2. Climatic and hygienic.—The infant has been badly clothed and exposed to cold and damp, or for many months together has lived in stuffy overheated rooms. The dwelling-house may be overcrowded, and the air constantly vitiated by the excretions of the dwellers. As a result, the infant suffers from bronchial and gastro-intestinal catarrh.

3. Congenital weakness.—Infants who are born prematurely, or whose parents are weakly, are more likely to suffer than vigorous and healthy infants.

With regard to the question of improper food, there is much perhaps that requires elucidation. Woman's milk, when produced under healthy conditions, is the only food suitable for an infant for the first eight or nine months of life, and the more nearly an artificial food approaches in composition to an average specimen of human milk, the more suitable it is for the wants of the infant. Woman's milk may from time to time be too rich or too poor in composition, and the infant may suffer in consequence, but such an infant suffers infinitely less than the infant fed on cow's milk or on one or more of the many varieties of tinned foods so readily procured.

Rickets has been attributed with more or less show of reason to the excessive use of starchy foods during the first year of life, to the use of

sweetened condensed milk, which contains an excessive quantity of sugar, while poor in fat and digestible proteids. Rickety infants usually do not waste and become atrophic, it is tolerably certain they can store away carbohydrates in the form of subcutaneous fat, but their digestion is readily overworked as regards the curd of cow's milk and perhaps also the fat; the curd of cow's milk is apt to decompose rather than digest in the infant's stomach and intestines, when the digestive powers are weak or a catarrh is present. But in the present state of our knowledge it is impossible to say in what way improper feeding produces rickets. It may be as stated, proteid-fat-starvation, or it is not at all improbable that the fermentation taking place in the alimentary canal forms bye-products or toxines, which being absorbed into the blood are responsible for some at least of the symptoms and phenomena of rickets.

Morbid anatomy.—The chief lesions found post-mortem in those dying during the active stage of the disease consist in very important changes in the bones, the conditions varying according to the stage and severity of the disease. As a rule, the bones which exhibit these changes most strikingly in the early stages are the bones forming the roof of the skull, the sternal ends of the ribs, and the lower end of the radius; and these bones should be examined carefully at the post-mortem, when rickets is believed to be present. These bones are the first to be affected, and show pathological changes in the early stages of the disease. Speaking generally, rickety bones are readily cut with a knife on account of the comparatively small amount of mineral matter they contain; they are softer and have much less rigidity and elasticity than normal bone. An examination of a rib in a case of severe rickets, say of a child in its second year, will show a considerable enlargement of the anterior end where it joins its cartilage, the swelling being, perhaps, more prominent on the pleural than cutaneous side; the rib will have lost most of its elasticity, it can be readily bent or, perhaps, " kinked " or snapped in two when sharply bent by the fingers. Section through the swelling made longitudinally will show the swelling to consist of cartilage, with islands of calcification and much red hæmorrhagic spongy bone on the rib side of the swelling. An examination of a radius may show a very striking enlargement of the lower end which involves the cartilaginous epiphyses and more or less of the adjoining shaft. Longitudinal section can readily be made by a strong knife through the enlarged carpal end, the swelling is made up (as noted in the rib) of cartilage, and a broad irregular zone of mixed calcified bone and cartilage. The centre of ossification in the epiphyses is usually not present in children under eighteen months of age. The shaft of the bone readily yields to pressure and bends, and if the rickety changes are well advanced, can be " kinked " or fractured between the fingers.

In explanation of these appearances, we must bear in mind that normal growth of bone—which is very active during the first two or three years— is effected, in length, by the proliferation of the cartilage cells and ossification proceeding at the ends of bones near the junction of the epiphyses and shaft; in thickness, by the formation of new compact bone around the shaft by the periosteum, while absorption is going on in the medullary cavity, increasing its size as growth proceeds. According to Quain, in the human subject, the growth of the long bones is chiefly in length, between the first and fourth years. The growth and nutrition of bone is profoundly disturbed in the active stages of severe rickets. The proliferating or growing zone at the ends of the bones—more especially the anterior

end of the ribs and carpal end of the radius—is immensely increased in depth and width, giving rise to the enlargement, while instead of true cancellous bone being formed, lime salts are deposited in an irregular and erratic manner, and irregular cavities are formed in the swollen cartilage containing grumous material. Beneath the periosteum marked changes take place, and instead of hard compact bone being formed, the outside ring of bone consists of partially calcified fibro-cellular tissue; if, then, as frequently takes place, there is an abnormal widening of the medullary canal, it is easy to understand how the bone loses its elasticity and readily bends and breaks.

The vault of the skull in a rickety child in the early stages is easy to remove at the post-mortem, as far as cutting through the bones is concerned. The bony tissue corresponding to the protuberances of the frontal and parietal bones is thicker than normal, but consists of cancellous-like spongy tissue, readily cut by a knife. The edges of the bones are also thickened, but are soft and cut quite easily, as there is often an almost complete absence of lime salts. The ridges on the occipital bone are well marked, and the bone is sometimes flattened in from pressure of lying on the back of the head. Cranio-tabes is more common before six months of age than after; it is seen mostly in the occipital bone or posterior part of the parietal. It is readily identified by stripping the dura mater off the occipital or parietal bone and holding it up to the light; small, translucent patches will be seen where the bone is thin or absent.

The subsequent changes which the bone undergoes depends upon the course of the disease. In the worst cases the bones remain for months, perhaps into the third year, in a soft and partially calcified state. They easily bend and undergo deformities, or they may be the subject of multiple fractures. If the rickety changes are severe, the growth of the bones is checked, the proliferating process at the ends of the long bones is interfered with, growth afterwards is slow, and the individual is certainly stunted. In the worst cases the abnormal curves, as those of the tibia in bow legs, remain, the bones harden by the deposition of lime, and the curve becomes permanent. In the slighter cases the swelling of the epiphyses gradually disappears, and the curves noted in the tibia and other bones gradually straighten out as growth proceeds, and tend towards normal.

Symptoms.—In the vast majority of cases of rickets, the first symptoms of the disease are noted during the second six months of life, or shortly after; though the results of rickets may be seen in the softness and deformities of the bones, with muscular weakness, long after this period, and indeed, as far as stunted limbs are concerned, throughout life. During the first six months of life, the activities of the infant, as far as muscular movements are concerned, are small; neither the muscles nor the ligaments or the bones of the limbs undergo much active development. But after this period has elapsed a marked development of the locomotive apparatus begins, the infant holds up its head firmly, gradually manages to sit up fairly well without support, and by the end of the first year is making vigorous attempts to crawl and get upon its legs. It is during this period of active development of the bones and voluntary muscles that rickets occurs, and it is the locomotive apparatus that is largely affected.

Early symptoms.—The early symptoms of the disease are indefinite, and in the slighter cases of rickets are either overlooked or are absent. The first characteristic sign of rickets is the enlargement of the epiphyses

of the ribs and bones of the wrist, and the thickening of the parietal and frontal eminences. But before these enlargements take place, or are well marked, the disease must have been in progress for some time, but the symptoms which occur during this period are mostly ill defined. One of the earliest symptoms which arouses suspicion of the onset of rickets, and which is always present in severe cases, is excessive sweating. This is most noticeable about the head and during sleep, but the perspiration is general, and often followed by plentiful crops of sudamina, which the mother probably describes as a " teething rash." Beads of perspiration may be seen to stand out on the infant's forehead, and its underclothes or night dress may become damp or wet. There is a notable restlessness of the infant during what should be the sleeping hours, it is uncomfortable, kicks off its clothes, and its nurse complains that it is a bad sleeper and requires constant attention and feeding at night. Its hair is often partially worn off the back of its head by its restlessness and rolling its head about. There is always a distended state of the intestines with gas, due to fermentative changes in the small intestine and stomach, with loss of tone of the muscular fibre of the intestines and abdominal walls; the abdomen looks large and round in consequence. It is probable also that the infant suffers from constipation, or the stools are large and putty-like. It is clear that these symptoms are due to gastro-intestinal dyspepsia, and the sweating suggests absorption of toxines from the alimentary canal. While the sweating and restlessness suggest the onset of rickets, if with these symptoms the appearance of the teeth is delayed, and the infant shows little disposition to muscular exertion, and makes no attempt to sit up or perhaps hold up its head when eight or nine months old, the suspicion of rickets will be confirmed. It many cases, at least, at this period, not only is there no attempt at sitting up and a backwardness in the use of its limbs, but it resents being moved and jumped about, and there is a certain indefinite tenderness of the bones of the limbs. Peritoneal tenderness is a sign of scurvy rather than rickets, but as scurvy so frequently occurs in conjunction with rickets, it is a noteworthy symptom.

Convulsions are among the early symptoms of rickets which may be present. The convulsions are usually frequent rather than severe, and are likely to be looked upon as teething fits. They are of the ordinary type of infantile convulsions, the clonic spasms, *i.e.* the muscular twitchings of the face and limbs being well marked, without perhaps any severe tonic spasms, *i.e.* stiffening of the limbs. There may be no obvious exciting cause, but this is usually to be found in the alimentary canal. Spasm of the glottis may occur in connection with the convulsive fits described later.

Characteristic signs.—It has already been remarked that in many cases, notably the less severe, the early symptoms are absent or overlooked, and it is only when there is obvious deformity of the bones that the disease is suspected. It may happen that a fat infant of a year old, entirely breast fed, showing signs of muscular weakness and enlarged epiphyses, is brought for medical advice, and no history of sweats or dyspepsia can be elicited. But in severe cases it is almost certain that what have already been described as early symptoms will be present. The *beading of the ribs* is mostly the earliest discoverable change in the bones, and it is almost constantly present. The anterior ends of the ribs where they join the cartilages are more or less swollen, and can be readily felt, and also seen if the infant is not too fat. The swelling involves both the pleural as well as the costal side, and indeed is often more prominent on

the former than the latter. This beading is mostly present at the eighth or ninth month, but may be often noted earlier than this. In addition to the beading of the ribs, a vertical depression or shallow groove is frequently present on each side of the sternum, involving a part of both ribs and cartilages, and caused by softening. The chest wall here is sucked in during inspiration, the sternum is thrust forward, increasing the antero-posterior diameter and diminishing the transverse. Any bronchial catarrh or obstruction to the air entering the chest will naturally tend to make the deformity worse. In some cases, instead of the above, a shallow transverse depression perhaps two inches broad is seen passing round the chest on a level with the tip of the sternum, and caused by the contractions of the diaphragm during inspiration, drawing in the softened ribs, and perhaps everting the lower edges of the chest wall (Harrison's sulcus).

The skull early shows change of shape due to rickets; there is thickening of the edges of the bones, and this is especially true of the parietal bones; there is a marked exaggeration of the frontal and parietal eminences, with a flattening of the vault of the skull, so that the head looks large and square. In some cases there are shallow grooves corresponding with the sagittal and coronal sutures, which give the top of the skull a "hot-cross-bun" appearance. The fontanelles are widely open long after they should be closing up. Less characteristic of rickets are the atrophic changes sometimes present, and which consist of small patches, more especially in the occipital bone, where the bone is thin or deficient, and can be compressed with the pressure of a finger. This atrophy of bone has been called cranio-tabes, and may be felt in very young infants; it is doubtful if it is always pathognomonic of rickets.

Sooner or later, in most cases, an enlargement of the epiphyses at the wrists takes place, and similar changes occur at the ankle, and also at the ends of the bones forming the knee. All these deformities are practically always symmetrical.

The soft flabby condition of the muscles is hardly less characteristic of the disease than the enlargement of the epiphyses. In some cases the muscular paresis and helplessness of the infant is the most noteworthy feature of the case. The infant at twelve months of age may be very helpless, and not offer to sit up at all by itself. At this time, if the case is at all severe, the infant presents a very characteristic appearance. The head is large and square, with widely open fontanelles; the gums are toothless, the ribs are beaded, the chest is narrow, the sides falling in during inspiration; the epiphyses at the wrists and ankles are enlarged. The abdomen is large and round from distension of the intestines with gas, and contrasts notably with the contracted chest. The muscles are soft, weak, and badly developed, and the infant cannot sit up, or does so with difficulty. The skin is moist, and perhaps covered with sudamina. In many cases the disease is far less well marked than this. The head may be fairly well formed, while the ribs are beaded, and the epiphyses enlarged; or the deformities not well marked, while the muscular weakness is excessive. Convulsions or laryngismus may be a marked feature of the case, or they may be entirely absent.

As the infant grows older, other deformities than those already mentioned make their appearance. On account of the deficiency of mineral matter, the long bones yield to pressure more easily than healthy ones, and curves or bends are produced. The ribs perhaps become bent or kinked at their angles, the clavicle in severe cases bends like a letter S, and

the edges of the scapula are thickened. The shafts of the bones of the limbs bend as they come to be used for sitting on the floor, or attempts at standing and crawling are made—the most marked being the tibia and fibula. The curves vary in position and degree, but usually the concavity is on the inner side (bow-legs), the lower part of the bone becoming turned inwards by the child sitting cross-legged on the floor. The femur usually bends with its convexity forwards or outwards, and the humerus may bend in a similar way. The bones of the forearm are less often misshapen; the curves usually are an exaggeration of the normal ones, and may be produced by the child crawling about the floor and resting some of its weight on the forearms. In the more severe cases of rickets the limbs are shorter than those of a healthy child, in consequence of the rickety changes in progress at the growing end of the bones; growth is interfered with, and the stature becomes stunted, while the hands and feet are often disproportionately large. In some Lancashire villages inhabited by a coal-mining or manufacturing population, large numbers of stunted bow-legged children will be seen in the streets, while the adult population, especially the men, are seen to be very much under the average height, some being actually dwarfs.

When the child has learnt to sit up perhaps at 18 months or 2 years of age, the spinal column is apt to give way on account of weakness of the ligaments and muscles, the natural curves becoming lost in a general bowing of the spine backwards (kyphosis), this backward curve extending from the upper dorsal to the lower lumbar. The curve is very apparent when the child sits up, and is straightened out if the child is suspended or by extending the spine.

The bones may not only bend but break in the severe forms of rickets. The fracture is usually of the " green-stick " variety, that is, the bone breaks and is " kinked " at the fracture, the ends being held together by the fibrous or non-calcified substance of the bone. The fractures are very likely to be multiple, being present at the angles of the ribs, clavicle, humerus, radius, or indeed any of the bones.

Rickets is essentially a chronic disease, and at best improvement is very slow, while in a large number of cases, especially where under unsuitable hygienic conditions, any decided improvement is long delayed. The more active phases of the disease, profuse sweating, restlessness at night, chronic dyspepsia, constipation, may perhaps be greatly improved in the course of a few months by careful dieting and residence in hospital, or still better at some seaside home. The muscular weakness, deformities of the epiphyses and shafts of the bone, do not so quickly disappear. That the ligaments are weak and more or less softness of the bones remain for a long time, is shown by the fact that knock-knees and flat feet develop after the child has been able to stand and also walk. Gradually, however, the bones consolidate, the head rounds off to a more normal shape, the swollen ends of the long bones become smaller, and the lesser degrees of curvature as in the tibia and fibula become less marked. The consolidation of rickety bones is often accompanied by an ivory-like condensation of the bone substance. In the worst cases the deformity of the shafts of the femur, tibia, and fibula become permanent unless their shape is restored by the surgeon.

Associated conditions.—Having given a sketch of the chief signs and symptoms characteristic of rickets, there remain to be described some associated conditions, which, though they form no essential part of the complaint, are often present:—

Bronchial catarrh.—It is exceedingly common among the out-patients of a children's hospital to see infants a year or more of age suffering from bronchial catarrh, and who show signs of rickets of moderate severity. The respiratory movements are increased in number, there is rhonchus and wheezing to be heard over the chest, the ribs are beaded, and the sides of the chest forming the anterior ends of the ribs are falling in at every inspiration. Undoubtedly the association of rickets and chronic bronchial catarrh is a very common one ; infants who are rickety are very sensitive to cold, readily get a bronchial catarrh, and the catarrh is very apt to be chronic. Then the bronchial attack disturbs the digestive organs, and entails close confinement to the house. Acute bronchitis and broncho-pneumonia are very fatal diseases in rickety infants on account of the want of rigidity of the chest walls, and the feeble power of the muscles of respiration.

Anæmia.—In most cases of rickets there is anæmia, and in severe cases the paleness of the infant is a very noticeable feature. Examinations of the blood have not hitherto yielded any very decided results, and the observations of different observers have been at variance. Hock and Schlesinger found a diminution in the number of red corpuscles (2,500,000 per c.mm.), and an increase in the number of the white corpuscles (15,000–40,000 per c.mm.). In connection with this it must be remembered that in infants and children generally the white corpuscles are proportionately more numerous than in adults. The same authors found an average of 60 per cent. of hæmoglobin with 2,300,000 cells. When the anæmia is at all severe, the spleen is usually enlarged. Rickety deformities are very frequently present in the anæmias of infancy, and while it is probable in some of these cases the rickets is secondary, it may be by no means certain in a given case whether rickets is the cause of the anæmia or secondary to it. Thus, in the condition known as anæmia infantum pseudoleukæmia there is grave anæmia, much enlarged spleen, moderate or extensive leucocytosis, and the majority of cases display enlarged epiphyses to a marked or moderate extent. When the anæmia is severe and the evidence of rickets slight, it is tolerably safe to assume that the rickets is secondary to the blood disease.

Laryngismus.—Reference has already been made to eclampsic attacks as often occurring in rickety infants among the early symptoms, perhaps before the enlarged epiphyses are very obvious. Child-crowing or laryngismus may also occur early in the disease, say at the eighth or ninth month or a few months later, and may persist for many months. The symptoms are due to spasm of the glottis; when the spasm of the adductors partially closes the glottis, inspiration is accompanied by a crowing sound; when, as sometimes happens, the spasm is complete, there is a momentary "catch in the breath," followed by evident distress and struggling; the infant becomes of a dusky colour, then the labouring inspiratory muscles succeed in forcing open the glottis with perhaps a long-drawn crowing breath. These attacks are commonest in those children who have been much confined to the house, and there is in some instances an attendant bronchial catarrh, while all are associated with rickety deformities and chronic indigestion. There are usually pale putty-like stools and much flatulence. The unstable condition of the respiratory centres is in all probably due to toxines absorbed from the alimentary canal.

Tetany is a form of tonic spasm affecting the limbs or muscles of the neck, mostly occurring in rickety children.

Enlargement of internal organs.—The liver is frequently enlarged in rickets, both in the early and late stages. In palpating the liver, care must be taken not to mistake the displacement downward of this organ—which often occurs when the chest is deformed—for enlargement. Enlargement is presumably connected with the indigestion so often present in rickets, and is no essential part of the disease. Reference has already been made to enlargement of the spleen in rickets; the enlargement is proportional to the anæmia present, and not to the severity of the rickets. The skull is often of a larger size than normal in rickets, due to thickening of the parietal and frontal bones; but in some cases at least the brain is above normal size and weight, though normal in appearance to the naked eye.

Scurvy.—Rickets coexists in many cases of infantile scurvy; it is not universally present, but in the experience of the writer the two are found associated together oftener than some recent writers will allow. In some cases of rickets of the severer type in the early stages, the bones are distinctly tender, and the child resents being moved, while at the same time there is no other evidence of scurvy present. In cases of severe rickets dying of broncho-pneumonia, we have frequently found tiny hæmorrhagic effusions on section through the ends of the swollen ribs. In these cases rickets was presumably associated with slight scurvy.

Dentition.—As a rule in rickets, dentition is delayed, perhaps no teeth making their appearance during the first year. It is not uncommon, however, to find that the lower two incisors are cut at the usual time, seven or eight months, and then a long delay ensues of many months. The order of appearance may be altered in rickets, as, for instance, the molars appearing before any of the lateral incisors, or the latter before the central incisors. It is usually said that dentition is apt to give rise to more trouble in rickety infants than it does in healthy ones, but this is only another way of saying that healthy infants are less troubled by tooth-getting than weakly ones. There seems to be no constant rule with regard to the condition of the teeth in rickety children when cut; certainly in severe rickets the teeth when cut are small and quickly become carious, and, on the other hand, in large numbers of children with slight rickets the teeth are good.

Chief deformities, Summary.—*Head.*—The skull bones are mostly affected when rickets occurs before the end of the first year; it is usually unaffected if rickets supervenes later. The frontal and parietal eminences become abnormally prominent, the edges of the bones are thickened, the upper surface of the skull is flattened, the shape of the head becomes square, with a circumference larger than normal.

Chest.—Beading of the ribs is an early symptom, and may be followed by deformities of the chest wall; there is a broad vertical groove on each side of the sternum, where the ribs and cartilages have fallen in, while the sternum and a portion of the cartilages have been thrust forward. Instead of the above, there is a broad transverse groove (Harrison's sulcus) on each side of the chest nearly on a level with the lip of the sternum, and corresponding with the attachment of the diaphragm. The lower edge of the chest wall is everted.

Upper limb.—In the clavicle there may be an exaggerated curve backwards at the outer and a similar curve forward at the inner end; the ends are thickened. The edges of the scapulæ may be thickened. The humerus may be bent, the convexity outwards, produced by the friends raising

the child by its arms; possibly the muscular action of the deltoid may also effect this. The radius and ulna may be affected in a similar manner, being bent outwards and twisted by the child crawling on all-fours.

Lower limb.—The deformities of the lower limb are more severe and more important than those of the upper, on account of the legs having to sustain the weight of the body. The chief deformities are the following:—

Coxa vara or a curvature of the neck of the femur downwards and forwards, the result of giving way in consequence of the femurs sustaining the weight of the body; as a result the leg is everted, and there is an awkward waddling gait; the trochanter is felt higher than usual, and the legs are shortened. Curvature of the shaft of the femur with the convexity forwards and outwards, with rotation of the lower half, overgrowth of the internal condyle and perhaps undergrowth of the external giving rise to knock-knees. Curvature of the shaft of the tibia, the convexity being outwards (bow legs); this may affect the tibia as a whole, or more especially the lower third. Rotation may also take place. Overgrowths on the tibia are common along the borders or at the internal condyle or immediately below it. Flat foot is very common; many of the deformities of the lower limb take place after the child has learnt to walk.

The rickety spine usually takes the form of a general curve backwards, *i.e. kyphosis,* affecting the whole dorso-lumbar region. In older children, after they have learnt to walk, the curvature may be *lateral* or in the form of *lordosis.*

Fœtal Rickets, Osteo-genesis Imperfecta, Achondro-plasia.

In rare cases, infants are born in a condition which suggests that they may have suffered from rickets during fœtal life. The limbs are stunted, the epiphyses swollen, the shafts of the bones curved, the ribs are beaded, and the chest misshapen as in rickets. There are often numerous fractures affecting the long, but also the scapulæ and other flat bones. Such children either are born dead or only survive their birth a short time. In a few of the cases, competent observers (Barling, Rotch) have described them as true rickets, which has taken place during intra-uterine life. In other cases the resemblance to rickets has been more apparent than real; in some of these there is a pug nose, broad head, and extremely stunted limbs, the latter being often only half their normal length. In such cases there has been an arrest of development during intra-uterine life of cartilaginous and perhaps also membranous ossification. Most of such cases are premature or still-born; a very few survive their birth, and grow up as dwarfs. The term achondro-plasia (Porak, J. Thomson) has been applied to this group. It is safe to say that many more observations are required before any very dogmatic statements can be made respecting these cases; for this reason they are perhaps best classed under the term of osteo-genesis imperfecta, which leaves the question of their nature an open one (Ballantyne).

Late Rickets.

Typical rickets, such as has been described in this article, only occurs during the first two, or at most three, years of life. Later than this period, when the parietal and occipital bones, epiphyses of the wrist, and other bones have undergone more complete ossification, the typical deformities of early rickets do not take place.

It is the universal experience that the changes which lead to the alteration in the shape of the head, beading of the ribs, rickety deformity of the chest, and bow legs, only occur at one period of life, namely, during the first two, or at most three, years.

It is, however, a common experience that older children, youths, and young adults, who have never suffered from rickets during the first year or two of their lives, do, after a more or less prolonged period of ill-health, exhibit symptoms, especially in connection with their muscles and ligaments, which suggest rickets. It has been said that these are cases of " relapsed rickets " rather than " late rickets," and this may be true of a certain number of cases, but it is pretty certain it is not true of all. Whichever view we take, it is clear that in a number of cases children of three or four years old and upwards, who have hitherto been fairly healthy, begin to show such symptoms as profuse sweating, muscular weakness, laxity of ligaments, overgrowth of bone at the epiphyses of the ankles and bones forming the knee-joints, resulting in more or less knock-knees, flat feet, and perhaps lateral curvature of the spine. These symptoms occur in rapidly growing children, but also in those who are growing very slowly. In some of these cases albuminuria occurs, but this is by no means constant. Such children are apt to have an ungainly and awkward-looking walk and carriage; they throw their feet out when they walk or run, giving way more or less at the knees and ankles, and loll about, drooping one or both shoulders from tiredness and weakness of the muscles of the back.

Mild cases of this class are common enough, while severe cases in which lateral deformities of the spine occur and bad knock-knees are far from uncommon. In rarer cases the child or young adult is unable to make any exertion, either walking or even sitting, and lapses perhaps for years into a complete invalid, spending most of his time in bed or on a couch.

Diagnosis.—It is not very often that there is much difficulty in diagnosing rickets, and there can be none if beading of the ribs, enlargement of the bones of the wrists, or the peculiar shape of the head, is present, these deformities being too obvious to be overlooked. In some cases, where the muscles of the trunk and legs are weak and the child very helpless as regards sitting up or standing, while there is no marked swelling of epiphyses of the wrists or obvious square looking head, there may be some doubt as to whether there is actual partial paralysis of the muscles, or weakness due to rickets. It must be borne in mind that beading of the ribs is seldom absent in rickets under two or three years of age, and if there is a general muscular weakness with beading of the ribs, the case is almost certainly one of rickets. Anterio-polio-myelitis is not likely to produce a general partial paralysis of the muscles of both legs. Moreover, there would be wasting and the reaction of degeneration present. In some cases the muscular weakness of rickets will—in a child who is able to walk—produce symptoms suggestive of an early or slight case of pseudo-hypertrophic paralysis. There is not likely to be any enlargement of the calf muscles, but the difficulty of rising from the floor, except with the help of the arms, suggests the more serious disease. The difficulties of diagnosis in connection with rickets are not so much as to whether the bone deformities due to rickets are present or absent, but to decide whether the rickets which is present is the primary and essential feature of the case. Undoubted rickets is often associated with gastro-intestinal indigestion, bronchial catarrh,

anæmia, imbecility, eclampsia, etc., but the question as to whether it is primary or secondary is frequently a difficult one.   Has the gastric catarrh or chronic bronchial catarrh present in an infant directly or indirectly caused the rickets?   Or has rickets predisposed to gastric and bronchial catarrh?   These questions do not always admit of a definite answer; possibly both questions may be answered in the affirmative. Rickets unquestionably predisposes to eclampsia and also anæmia, but in a given case there may be some other factor causing the eclampsia and the anæmia, and the rickets may be only secondary.   In these cases, if the bone deformities are slight, rickets is hardly likely to be the essential cause.   Imbecile and feeble-minded children may be rickety, but while severe cases of rickets are often mentally backward, the presence of rickets will not account for idiocy or imbecility.   The hydrocephalic head of the infant ought not to be confused with the large square head frequently seen in rickets.   In the former, the enlarged head is globular, the fontanelles bulging, the bones of the skull thin; in the latter, the head is square and flat at the top, the frontal and parietal eminences prominent, the edges of the bones thickened; the fontanelles do not bulge.

Treatment.—If rickets is due to dietetic causes, *i.e.* mal-digestion and mal-assimilation of food and possibly also to the absorption of toxines from the alimentary canal, it is clear that the most important therapeutative measures will be those which aim at improving the digestive powers and supplying food of suitable quality and in suitable quantity.   In any case in which the early symptoms of the disease, such as sweating, restlessness, prominent abdomen, beaded ribs, have manifested themselves, the diet and general hygiene of the infant should be carefully regulated.   It will almost certainly be found that there has been chronic dyspepsia in progress for some time, that the digestive powers have been seriously weakened, and that the infant cannot take and digest the amount of food which a healthy infant can.   The gastric and intestinal juices are weak, the bile is poor in quality, the muscles of the stomach and intestines have lost much of their tone, the blood is poor and watery.   The digestive juices are weak because the blood is poor and thin, and the blood is likely to remain poor if the digestive powers are weak.   It is clear, then, that no rapid improvement can be expected, and the digestive organs will have to be gradually "coaxed back" to a normal condition.   With the early symptoms of rickets just referred to, it will probably be found that the infant's stools are pale and putty-like and perhaps foul smelling.   Or they may be pale and dry, so much so that they can be broken, or they come away in pieces. The infant is probably taking far more curd of milk than it can digest; the curd is partly undergoing decomposition in the alimentary canal and in part being passed in the stools.   The almost total absence of yellow colour in the stools suggests that an insufficiency of bile is being secreted, and probably also the digestive juices are weak; the peristalsis of the bowels is very inefficiently performed.   Possibly with this state of things we find that the infant has suffered a good deal and is suffering from bronchial catarrh, or it has more or less "child crowing," and as a result it is carefully kept day after day in a close apartment, without fresh air, and perhaps a steam-kettle constantly puffing wet steam into the room.   The indications for treatment will naturally be to find a food which the infant can digest, which contains the necessary proteids, fat, etc., and at the same time to ensure that the infant gets an amount of fresh air and sunlight which is as necessary to it as its food and drink.   With regard to food, each

case will have to be treated on its merits, and carefully watched to see how digestion proceeds. Avoid a one-sided diet. The diet should contain proteids, fats, sugars, salts, and there is no harm in starches in small quantities, if the infant, as it probably will be, is over 8 or 9 months old. Prefer fresh food to preserved food as far as possible, at any rate make sure there is a sufficiency of fresh food in its diet, or scurvy is very likely to be set up. Whey made with Benger's rennet, to which, after scalding, a fourth part milk or a smaller quantity of fresh cream is added, may be given. If with this the stools are pale and contain curd, raw beef juice may be added in place of milk. A little thin and well-boiled oatmeal made with whey or milk and water may be given, with or without the addition of malt extract before being taken. No thick foods are permissible before the age of a year. Plasmon dissolved in barley water or whey is certainly of use in some cases for supplying proteid; if given in barley water it will be well to give some orange juice daily, and, indeed, this may be given in all cases of rickets, especially when it has become necessary to reduce the quantity of milk. Where milk laboratories are available, a milk food may be ordered with the proteid kept low at first, 0·75 to 1·5 per cent., fat in moderately large amounts, 3 to 4 per cent., and sugar, 5 to 6 per cent. The amount to be taken to be 35 to 40 oz. in the twenty-four hours. To attain much success in the treatment of such a case, very careful watching is necessary. It may be necessary from time to time to cut down the strength of the food or to gradually increase it.

The diet of older children, say 18 months to 2 or 2½ years, must be managed in a similar way. Watch the stools. It is quite certain if the stools are putty-like and foul, the child is not doing well. Reduce the curd the child is taking by giving whey, and substituting beef-tea, chicken tea, raw beef, etc., for some of the milk. Thin well-boiled oatmeal porridge and cream, yolk of egg, slackly boiled, on sopped toast, sandwiches made with thin bread and butter and egg or underdone beef, or bone marrow may be given in small quantities. Scraped raw beef or underdone beef is of undoubted value in rickets, but the quality of the beef requires most careful supervising, as the risk of the child becoming the host of a tapeworm is by no means small if there is any carelessness in the selection of the meat. Proteids and fats the child undoubtedly requires, but milk is apt to disagree in many cases of rickets, and the difficulty often consists in finding suitable and easily digested proteids. An excess of curd of milk given may mean not only proteid-starvation but toxine-poisoning.

The importance of fresh air in the treatment of rickets cannot be overestimated, it is just as important in this disease as in the treatment of tuberculosis. The worst cases to treat are those who are subject to bronchial catarrh, especially during the winter months. The treatment of rickets is mostly unsatisfactory in hospital, unless there is opportunity of sending the infants daily into the open air. Whenever it is possible and the weather is fit, let the infant spend the whole day in the open air, and take its meals outside. During the six months of winter, a seaside place with a sandy shore, and where shelter from high winds can be obtained, is far more suitable for a rickety infant than a city or inland resort. Great care must naturally be taken not to over-expose the rickety infant, who easily gets bronchial catarrh, but too much coddling is bad, and renders the infant too much of a hot-house plant, and too sensitive to outside air. Use them gradually to fresh air, by admitting the air to the bedrooms, when the infant is suitably dressed.

It is of course necessary to very carefully attend to the clothing of sensitive children. Shetland wool vests, abdominal belts of the same material, woollen or flannel outer clothing, gamgee tissue napkins, and suitable wraps when the infant goes out. Keep the feet warm with a hot-water bottle at the foot of the carriage when the child goes out in cold weather. In severe cases the most careful handling is necessary, as fractures easily take place, and the prone position on a soft mattress or cushion in the cot or carriage is better than much nursing in the arms or sitting up in a chair, on account of weakness of the back. Much difficulty is experienced in keeping the child off its feet or attempting to stand or crawl, whilst the bones of the legs are still more or less soft and the ligaments of the joints weak. Such children want amusing during their waking hours, and much ingenuity and patience must often be exercised to keep them off their feet.

Of medicines the most important are those which assist digestion or overcome faulty conditions of the mucous membrane of the stomach and bowels. The troublesome constipation also requires attention. From time to time a dose of calomel ($\frac{1}{2}$ to 1 gr.) is useful to carry away accumulations of decomposing and fermenting food. Acids and pepsin are useful in many cases—Acid. nitrici dil., 1 minim; liq. pepsin and euonymin, 20 minims; aq. lauro-cerasi, 5 minims; sp. chloroformi, 1 minim; aq. aurantii flor. ad 1 dr.　1 dr. *t.d.s.*—Infant 8 months to 18 months.

If there is constipation and much gaseous distension of the abdomen, soda and rhubarb is often of value, given in small and repeated doses for a week or two—Sod. bicarb., 2 gr.; pulv. rhei, $\frac{1}{4}$–$\frac{1}{2}$ gr.; sp. chloroformi, 1 minim; syrup. pruni virgin., 15 minims; aq. ad 1 dr.　1 dr. *t.d.s.*—Infant, to 18 months.

Glycerin or oil enemas may be necessary from time to time to get the bowels to act. Cod-liver oil is of undoubted service, especially in the form of emulsion, where the digestive organs are comparatively healthy; it is better not given if there is much dyspepsia. Iron and arsenic are of some value in the anæmic cases, the former as iron-somatose or Hömmel's hæmatogen, and the latter in the form of Levico water. Phosphorus has been vaunted as a specific; it is however, very little used at the present time, and has deservedly fallen into disrepute.

Cases of laryngismus are often troublesome, and it may be some weeks or even months before the tendency to laryngeal spasm and convulsions is overcome. The most important matter to be attended to is the diet, for it is almost certain to be at fault. Then fresh air, preferably seaside, is of the greatest importance; but as sudden death from spasm of the glottis takes place at times, it may not be always wise to send them away from home to the seaside. Calomel and phenacetin (āā 1 gr.) may be given to clear out the bowels, the latter given as a nerve sedative. Bromide and rhubarb may be given—pot. bromid., $2\frac{1}{2}$ gr.; pulv. rhei, $\frac{1}{4}$ gr.; sp. chloroformi, 1 minim; syrup. aurant., 20 minims; aq. ad 1 dr.　1 dr. *t.d.s.*—Infant 8 months to 1 year.) Perhaps the best antispasmodic in severe cases is morphine given subcutaneously in $\frac{1}{100}$ to $\frac{1}{50}$ gr. doses, or chloral hydrate given in doses of 2 or 3 gr.—Infant 8 months to 2 years.

The treatment of rickety deformities mostly falls to the surgeon, and splints or osteotomies may be required, but a good deal can be done to improve the muscular power by massage and baths, and by daily gentle manipulation to straighten curved tibiæ, if it is persistently practised before the bones have become firmly set in a faulty position.

The treatment of rickets does not consist in prescribing "chemical

food" or cod-liver oil, but in carefully studying the digestive powers of the individual infant and giving it a generous supply of fresh air.

HENRY ASHBY.

FRAGILITAS OSSIUM.

FRAGILITAS OSSIUM signifies an abnormal brittleness of the bones; it is applied to cases in which fractures take place as the result of slight accidents or muscular action. The term is applied to two fairly distinct classes of cases—(1) A rare condition, in which brittleness of the bones exists, unconnected with any other well-known disease; usually the subjects are in good health. (2) An abnormal brittleness of the bones, which is the result of some disease, as rickets or scurvy.

Etiology.—The idiopathic form is in some cases hereditary, and several members of the same family may be affected; there is a family tendency to fractures, which may be comparatively slight or very unmistakable. Greenish records a remarkable instance of this hereditary tendency to fracture. The grandfather of the family was an invalid, from numerous fractures. Of his three sons, one had one fracture; and of this son's children, one had thirteen and another two. The second son had two fractures; and of his children, one had eight, three had four each, and one had three. The third son and two daughters had no fractures.

Disease of limbs, as from lying in bed for many months, is apt to lead to atrophy of bone and consequent brittleness. The ease with which the bones of lunatics fracture is well known; doubtless in these cases atrophy of bone occurs.

It is an important fact, first pointed out by Magitot, that workers in match factories, where yellow phosphorus is used, seem abnormally liable to fractures of their long bones. Cases have been reported by Gorman and Dearden in this country, and by several Continental writers.

In the secondary form the fragility of the bones is obviously the result of some diseased or morbid condition; thus, for instance, it occurs in malignant tumours of bone, rickets, scurvy, purpura, atrophy of bone, osteo-malacia, phosphorus poisoning.

Symptoms.—The first fracture usually occurs during early life, perhaps about or before puberty; boys appear to suffer much more than girls. The bone perhaps breaks with ridiculous ease, as for instance a fracture of the humerus occurs when in the act of throwing a cricket ball, or a leg is twisted, and the femur snaps. There is no bending of the bone as in osteo-malacia, and no greenstick fracture. Union takes place usually without any difficulty, though exceptions to this have been reported. As the individual gets older, other fractures of the bones of the leg or arm, clavicle or ribs, occur, and deformity of the limbs may take place in consequence. The individuals appear to enjoy good health. The cause is unknown, and examination of the bones has not thrown any light on the subject.

Infants occasionally suffer fracture of their bones during parturition or during intra-uterine life. In some of these cases there is evidently disease of the bones (see "Foetal Rickets," p. 498). In others there is no obvious disease to be made out. Thus in an infant 2 weeks old, admitted into the Manchester Children's Hospital, both humeri and one femur had been fractured during labour. Splints were applied, and union took place;

during its stay in the hospital the other femur fractured in the middle third, without any obvious violence or accident. The infant seemed healthy; there were no enlarged epiphyses, but the ribs were slightly beaded, and the occipital bone flattened from lying on its back.

Diagnosis.—In rickets the fracture is usually of the greenstick variety; in scurvy it is usually a separation of the epiphysis, especially at the lower end of the femur. In one case, seen by the writer, this latter accident occurred while the infant (11 months) was being bathed. In another case of a child of 14 months, suffering from anæmia, and both rickets and scurvy, fractures of both humeri took place; the fractures were oblique and complete, there was much effusion of blood beneath the periosteum; this was verified at the post-mortem, death taking place a few weeks after the accident. The fractures had apparently occurred as the result of holding both arms of the child, and shaking it to stop its crying. In some cases of anæmia and purpura with malnutrition in older children, the bones become brittle and readily break. The writer has made more than one post-mortem examination of children in whom there were bruise marks, internal hæmorrhages, and multiple fractures, which suggested cruelty on the part of the parents; but an examination showed the bones, especially the ribs, were soft and readily broken by slight violence.

<div align="right">HENRY ASHBY.</div>

OSTEO-MALACIA—MOLLITIES OSSIUM.

OSTEO-MALACIA, as the name implies, signifies softening of the bones. In typical cases it is a well-defined disease, but in some other cases, in which more or less decalcification of bones occurs in early life, there is a difficulty in deciding whether to include them under the term osteomalacia or not.

Etiology and morbid anatomy.—In typical cases the disease occurs in women—men but rarely—between the ages of 25 and 35; pregnancy seems to be an exciting cause.

The bones are the only part of the body that appear to be affected. The early stages of the disease appear to consist in a gradual decalcification of the bones, leaving the animal matter intact. Later, the decalcified bone is gradually converted into a grumous blood-stained jelly, with perhaps some thin layer of firmer substance beneath the periosteum.

Symptoms.—Adult form.—In the early stages, pains in the bones, which are assumed to be rheumatic, are felt, but in many cases the first symptoms are those connected with the bending of the long bones or pelvis. Frequently the first bone to be affected is the pelvis, the deformed pelvis being discovered per vaginam by the accoucheur; the cavity of the pelvis is narrowed by the sides falling in and the sacrum being thrust forward. The deformity may be confined to the pelvis; usually other bones are also affected. It may be noticed that the stature is diminished, in consequence of the femurs bending; or the bones of the arms can be bent by manipulation into all sorts of curves, or may fracture. The chest and spine may become deformed.

The disease is mostly chronic, and goes on for years; the patient is bedridden and helpless, and perhaps finally dies of asthenia, or in consequence of the softening of the ribs preventing the expansion of the chest.

Juvenile form.—While the diagnosis in cases just described cannot be difficult, there is a great deal of uncertainty with regard to certain cases of bone softening which occur during early life. In some cases of newly born infants, the bones readily bend, in consequence of a deficiency of mineral matter, without, at the same time, there being any epiphyseal over-growth, as in rickets. Judson Bury records a case of an infant born with bent limbs, which died when 8 months old. At the post-mortem examination, it was found that the bones could be bent with the greatest ease, and it required great care to remove a rib without breaking it; the tibia and other bones were easily cut with a knife, and consisted of a mere shell of bone beneath the periosteum, while the interior of the shaft was filled with soft pulpy tissue. There were no enlarged epiphyses or evidence of rickets. Similar cases occur both in infants and young adults.

Treatment.—No known remedy appears to have any influence over the disease. The treatment is that of symptoms.

<div align="right">HENRY ASHBY.</div>

DIABETES MELLITUS

DIABETES MELLITUS is a disease in which there is persistent excretion of grape sugar in the urine. The term glycosuria is usually applied to the condition in which there is a temporary excretion of grape sugar in the urine; and in such cases the sugar excretion is usually small. But some writers also apply the term chronic glycosuria to the mild cases of persistent sugar excretion (mild forms of diabetes mellitus), and reserve the term diabetes for the severe forms.

Physiological considerations.—The carbohydrate products of digestion are conveyed to the liver, and this organ contains glycogen, which is present in greatest quantity when a carbohydrate diet is taken. It is still a disputed point whether the function of the liver is to constantly pay out small quantities of sugar into the general circulation, or whether the liver and intestinal villi act in the opposite manner and prevent sugar entering the general circulation, as Pavy suggests. If, in the normal condition, sugar were constantly passing into the general circulation from the liver, Pavy thinks that it would be detected in quantity in the urine: he believes that any excess of sugar in the blood is eliminated by the kidneys. But whatever the function of the liver may be, the blood does contain a very small quantity of sugar. Minkowski has shown that excision of the liver causes the sugar in the blood to disappear; and the same result has been obtained by ligature of the blood vessels of the liver (Bock, Hoffmann, Seegen). Glycosuria was not produced by the intravenous injection of large quantities of sugar in the experiments of Biedl and Kraus. Also glycosuria was not produced by the subcutaneous injection of dextrose, lævulose, and galactose in the experiments of Voit; but after the injection of cane and milk sugar the whole of these substances were excreted in the urine.

Experimental diabetes and glycosuria.—Diabetes or glycosuria has been produced in animals by experimental lesions of various parts of the nervous system: puncture of the floor of the fourth ventricle (Claude Bernard), division of the medulla (Pavy), injury of the vermiform process of the cerebellum (Eckhard), injury of the pons and posterior columns of the

spinal cord (Schiff), centrifugal vagus irritation (Arthand and Buttc). By the injection of defibrinated arterial blood into the portal vein, diabetes was produced by Pavy.

It has been shown by Minkowski and v. Mering, de Dominicis, and others, that total extirpation of the pancreas in animals is followed by diabetes mellitus. If a portion of the pancreas ($\frac{1}{4}$ to $\frac{1}{8}$) be left in the abdomen, diabetes does not occur. Also Minkowski has shown that a portion of pancreas, grafted under the skin of the abdominal wall, will prevent the occurrence of diabetes, when the whole of the gland is removed from the interior of the abdomen; but if this graft be subsequently excised, then diabetes is produced. It appears probable that in the normal condition an "internal secretion" is absorbed from the pancreas, which has a sugar-destroying action (Lépine).

Glycosuria.—In addition to true diabetes, or permanent glycosuria, cases are often met with in which sugar is present in the urine for a short time only—temporary glcosuria.

In health, the power of sugar-destruction in the system is not un-limited, and if very large quantities of sugar be taken, slight glycosuria occurs. According to v. Noorden, 150–200 grms. of cane sugar, 180–250 of grape sugar, or 120 of milk sugar, when given in one quantity on an empty stomach, will cause sugar to appear in the urine in a healthy person. In various diseases, and in apparently healthy persons, the power of sugar-destruction is sometimes much diminished. This has been noted in some cases of Graves's disease, cirrhosis of the liver, chronic alcoholism, obesity, etc.

As a test for diminution of the power of sugar-destruction, 100 grms. of dextrose may be given two hours after a breakfast of coffee and bread. If a decided reaction for sugar is obtained afterwards in the urine, the sugar-destroying power of the system is diminished (Naunyn).

It has been shown that in the puerperal state, milk sugar (lactose) is usually present in the urine at some period. Glycosuria, with increase in the quantity and specific gravity of the urine, may be produced, both in man and in animals, by the administration of phloridzin by mouth or hypodermically (phloridzin diabetes). Other substances sometimes pro-duce slight glycosuria when taken in toxic doses; for example, opium, chloral, hydrocyanic acid, arsenic, phosphorus, uranium salts, etc.; chloro-form and ether narcosis also occasionally, but not invariably, produce slight temporary glycosuria.

Slight glycosuria occurs sometimes after injuries to the head and fractures of the skull; it is occasionally, though very rarely, associated with brain affections, such as cerebral hæmorrhage, meningitis, tumour of the brain (exceedingly rare), or, in very rare instances, with other diseases of the nervous system, such as disseminated sclerosis, locomotor ataxia, or Graves's disease. Occasionally it occurs for a short period after various fevers—typhoid, scarlet fever, and diphtheria. A few cases are on record in which pentose has been present in the urine, and has given rise to a reduction of Fehling's solution, but no definite symptoms have been observed in these cases.

Etiology.—Diabetes is not a common disease. At the Manchester Royal Infirmary in twenty years there were 272 diabetic cases amongst 27,721 medical in-patients, *i.e.* 0·9 per cent. In England, France, Denmark, and the United States, the mortality from diabetes is steadily increasing. The German view is especially prone to diabetes. In India,

chiefly amongst the Hindus, in Ceylon, South Italy, and Malta, the disease is met with more frequently than in other countries.

The disease is more frequent in males than females. It is more common in adults, though cases are met with in young persons and children. The death-rate from diabetes is greatest after 40.

Predisposing and exciting causes.—There are a number of predisposing or exciting causes which sometimes appear to play a part in determining the onset of the disease, though it is probable that there is always some additional unknown factor in the causation. The following are the more important; and the percentages amongst 100 diabetic patients examined by the writer, in which there was a history of these predisposing or exciting causes, is given in brackets.

A family history of the disease is sometimes obtained. A brother or sister may have been diabetic also; sometimes an uncle or aunt; very rarely has the father or mother suffered. In 13 per cent. of the writer's cases a family history was obtained. In one instance two brothers and a sister died of diabetes; in another, three sisters suffered from it. A severe external injury, usually of the head, has been the exciting cause in a few cases, 6 per cent.. Many instances are on record in which the disease has rapidly followed fright, violent passion, strong mental emotions, mental anxiety and worry, 10 per cent. Mental anxiety and over-work, connected with the nursing of a sick relative, appears sometimes to be an exciting cause, 8 per cent. Alcoholism—usually excessive beer-drinking—probably predisposes to the disease, 17 per cent. Diabetes has occasionally developed directly after an acute illness, such as influenza, 8 per cent.; acute fevers, pneumonia, bronchitis, pleurisy, after exposure to wet and cold, after the taking of a large quantity of cold fluid when the body has been very hot. Possibly syphilis may be occasionally an indirect cause of diabetes, by producing cerebral or pancreatic lesions. In cases of acromegaly, diabetes or glycosuria often develops. Occasionally diabetes commences during pregnancy, 6 per cent. It has been suggested that the climacteric period predisposes to the development of diabetes in women. Mild forms of diabetes are sometimes associated with gout or obesity, 4 per cent., especially in elderly persons. In young persons, marked obesity has occasionally preceded a severe form of the disease. Often no history of any exciting or predisposing cause can be obtained.

Pathology.—Diabetes mellitus has no characteristic morbid anatomy. Often the morbid anatomical or histological changes are slight, and due only to complications; but in some cases changes are found in the pancreas or brain which are probably the cause of the disease.

The condition of the blood will be described in the section on symptomatology. The heart is often small and atrophied in severe cases; but cardiac hypertrophy is sometimes found. The cardiac muscle sometimes presents fatty or glycogenic degeneration.

The lungs present signs of tuberculous phthisis, early or advanced, in about half of the autopsies on diabetic hospital patients. The lung affection runs a rapid course; caseation soon occurs, and cavities form; there is no tendency to cicatrisation. Occasionally chronic pneumonic gangrene, broncho- and croupous pneumonia, are met with.

No important changes are found in the alimentary canal. Occasionally tuberculous ulceration of the intestines has been present. The liver is often enlarged, in other cases normal or diminished in size. Congestion,

fatty infiltration, and cirrhosis are occasionally found.   Multiple abscesses were present in one of the writer's cases.

Changes are often found in the pancreas.   The condition of the pancreas in twenty-four cases examined by me was as follows :—

	Cases.
(a) Extensive changes (marked cirrhosis 2, cancer 1, very marked atrophy 1)	4
(b) Well-marked changes (cirrhosis 2, lipomatosis 1, atrophy with fatty degeneration and infiltration 1)	4
(c) Slight changes (atrophy with fatty degeneration 1, atrophy out of proportion to the general wasting 2) . . .	3
(d) Atrophy, but only corresponding to the general wasting .	5
(e) Normal, macroscopically and microscopically . . .	8
	24

Marked atrophy has often been recorded; sometimes the gland tissue has been almost completely destroyed by cirrhosis or by fatty degeneration and infiltration; pancreatic calculi with fibroid change, and pancreatic cysts have been also found. Occasionally there has been advanced arteriosclerosis of the pancreatic vessels, which has apparently been the cause of the pancreatic changes.

The kidneys are often hypertrophied, in other cases they are normal macroscopically. Changes are frequently present in the renal epithelium : hyaline degeneration, necrosis of epithelium, fatty degeneration, glycogenic degeneration, chiefly in the loop of Henle. Occasionally chronic nephritis (parenchymatous or interstitial) is present as a complication.

The brain is often normal, or presents only changes which are slight or due to complications; but sometimes lesions are found which are probably the cause of diabetes, such as tumour, softening, fatty degeneration, sclerosis, cysticercus, etc., in the floor of the fourth ventricle; tumour of the medulla and of the base of the brain; tumour compressing the vagus nerve. In five out of ten cases examined microscopically by the writer, there was well-marked dilatation of the small blood vessels in the vagus nucleus, but in the other five cases no changes of importance were detected. Tumour of the pituitary body has often caused diabetes or glycosuria, with or without symptoms of acromegaly.

The spinal cord is usually normal, but the writer has found degenerative changes in the posterior columns in two cases, probably the result of the altered blood condition ; other similar cases have been recorded. In a very few cases, lesions of the cervical region of the cord (tumour or softening) have been found, which may have played some part in the causation of the diabetes.

Pathogenesis.—There can be no doubt, at least in the majority of cases, that sugar appears in the urine on account of the excess of sugar in the blood, and the symptoms of the disease are due to the same cause. The increased amount of sugar in the blood is believed by some writers to be due to excessive sugar production in the organism; by others, to diminished sugar destruction, or to diminished destruction in some cases and increased production in other cases. Limited space forbids a discussion of the conflicting views on this subject.

In the mild forms the sugar in the urine appears to be derived directly or indirectly from the carbohydrates of the food, since a rigid diet, free from those substances, causes the glycosuria to cease. Seegen believes that

in these cases the liver cells are unable to transform the carbohydrates normally. According to Pavy, there are two lines of defence, the cells of the intestinal villi and the liver. If synthesis of the carbohydrates derived from the diet is not performed at these two defence lines in a normal manner, sugar reaches the general circulation in abnormal quantities, and appears in the urine. In the severe forms of the disease, however, the sugar excretion continues when the diet is free from carbohydrates, and even when no food is taken. In these cases it appears probable that sugar is produced from the proteids of the body (as suggested by Pavy and others).

Whether we accept the view of increased sugar formation, or diminished sugar destruction, as the cause of the excess of sugar in the blood, we have still to consider why this abnormality should occur.

There is strong evidence in favour of some change in the central nervous system being the starting-point of the disease in certain cases. As already mentioned, occasionally the disease has immediately followed a severe mental shock or fright. Experiments on animals have shown that injury to the floor of the fourth ventricle, and other parts of the medulla and base of the brain, will produce diabetes mellitus. Post-mortem examination in patients dying of diabetes has sometimes revealed changes in the floor of the fourth ventricle, in the medulla, or base of the brain, as already mentioned. Undoubtedly examination of the nervous system, including microscopical examination of the medulla, reveals no very definite changes in the majority of cases. But it is still possible that minute changes may be sometimes present in the nerve cells of the vagus nucleus or other parts of the medulla, which cannot be recognised at present by microscopical examination. Pavy has suggested vasomotor paralysis and dilatation of the small vessels of the liver as the cause of diabetes, but this view has been criticised by Seegen.

Experiments on animals show, as already mentioned, that total extirpation of the pancreas produces diabetes. Post-mortem examination of diabetic patients has often revealed extensive changes in the pancreas; and there can be little doubt that these changes have been the cause of the disease, when there has been very marked destruction of the pancreatic tissue (as in group (*a*) of twenty-four cases tabulated). But in other cases the pancreas is normal macroscopically and microscopically (eight of the twenty-four cases tabulated), and in such cases diabetes has been due to lesion of other parts, or, if due to pancreatic affection, the disease must have been a functional one, giving rise to no histological changes.

Probably atheroma is the cause of a few cases of diabetes, by producing marked disease of the pancreatic vessels and consequent extensive fatty or fibrous changes in the pancreatic tissue. The changes which are found in the liver cannot, in the majority of cases, be regarded as playing any part in the causation of the disease, since similar changes are so frequently met with when there have been no symptoms of diabetes during life. Bunge and others have suggested that diabetes may be the result of some pathological chemical changes occurring in the muscles in certain cases.

It appears probable that the starting-point of the disease is not always the same. In many cases there is no history of any exciting cause, and the pathological examination fails to reveal any lesion in the brain, pancreas, liver, or other parts to which the disease can be attributed.

Symptoms.—Onset.—The first signs of the disease are usually thirst and diuresis, sometimes cramps in the calf muscles at night: or

the patient may seek medical advice on account of weakness and loss of flesh, or on account of one of the complications (eczema of the genital organs, gangrene, carbuncle, cataract, etc.). Apparently the thirst occasionally commences very suddenly. Sometimes very slight glycosuria has been detected months or years before the onset of true diabetes.

External appearance.—In severe forms the face is often wasted, the wrinkles and naso-labial folds are prominent, but there is not marked anæmia unless some complication be present. In milder forms there is nothing peculiar in the expression. General wasting of the body is a prominent symptom in severe forms; but in elderly patients, suffering from mild forms of diabetes, obesity is not infrequent. In severe forms the patient often complains most of general weakness.

Urine.—The quantity is increased—in severe cases greatly (150–250 oz. daily), in mild cases slightly. The colour is pale, usually straw-coloured; often, but not always, the tint is slightly greenish yellow. In the very mild forms the colour is normal. The urine is usually clear, and a mucous cloud, when present, often floats to the top of the urine glass. In diabetic females the urine is often turbid, owing to the presence of pus and epithelial cells from the vulva. The reaction is nearly always acid. The specific gravity is above the normal, and may reach 1030, 1045, or more. In very mild cases, and in temporary glycosuria, the specific gravity may be normal or even subnormal. The most important change in the urine is the presence of grape sugar. The amount of sugar present varies according to the severity of the case, from 0·5 up to 8 or 10 per cent.; and the daily excretion may reach 2000 or 3000 grs. or more. The patient frequently notices that flies are attracted to his urine, and that if a drop of it should fall on any object and be allowed to dry a white deposit is left behind.

The sugar excretion is increased by food—diminished by fasting. In many mild cases the excretion during the night is very small, or the night urine, passed before breakfast, may be free from sugar; whilst the day urine contains a large quantity of sugar. The sugar excretion is increased by carbohydrate food, but diminished by a nitrogenous diet. In mild cases, withdrawal, or sometimes even restriction, of the carbohydrates of the diet causes the glycosuria to disappear; but in severe cases the most rigid nitrogenous diet, and even fasting, fails to remove the glycosuria. Of the carbohydrate articles of diet, grape sugar causes the greatest sugar excretion, fruit sugar (lævulose) is only half as injurious, whilst milk sugar and cane sugar occupy a position midway. Starch is much less injurious than sugar. Fats and moderate quantities of alcohol do not increase the sugar excretion. Muscular exercise diminishes the sugar excretion in mild cases, but increases it in the severe forms with wasting. The glycosuria and other diabetic symptoms are diminished or arrested by intercurrent affections. When phthisis occurs as a complication, the sugar excretion may cease just before the fatal termination.

Albuminuria is usually absent at first, but often appears at a late stage —in 44 per cent. of cases. Usually, however, the amount of albumin is very small, and is not associated with nephritis; in a few cases it is more abundant, and due to chronic parenchymatous or interstitial nephritis. Owing to the excess of nitrogenous food, the urea excretion is increased; in a few cases only is the increase due to destruction of the albumin of the body. Sometimes there is an abundant deposit of oxalate of lime in the urine glass; in mild cases, there is frequently a deposit of uric acid crystals. In the most severe forms of the disease, the addition of a solution of

perchloride of iron to the urine often produces a dark brownish red coloration (Gerhardt's reaction), which is probably due to the presence of diacetic acid or some closely allied body. The urine often contains acetone, and β-oxybutyric acid is frequently present in the severe forms at a late stage.

The blood.—Normal blood contains a very small quantity of sugar— from 1 to 1·7 per 1000 (Pavy, Seegen). In diabetes mellitus the amount is increased, often markedly—it may reach 2·7 to 5·7 per 1000. A milky condition of the blood has occasionally been noted on post-mortem examination, and in some cases a milky serum has separated when the blood has been kept for some time. This condition has been shown to be due to excess of fat.

The writer has discovered a simple method of distinguishing diabetic blood from non-diabetic blood. A drop of blood taken from the finger is sufficient to give the reaction. About 40 c.mm. of water are placed at the bottom of a small narrow test-tube. The patient's finger is pricked and 20 c.mm. of blood are added to the water in the test-tube. The capillary tube of a Gowers' hæmoglobinometer may be used for taking the blood from the pricked finger. Then 1 c.c. (1000 c.mm.) of a watery solution of methylene-blue (1 in 6000) is added, and finally 40 c.mm. of liquor potassæ (B.P.). The fluids in the tube are well mixed. As a control experiment a second tube is used, containing the same quantity of non-diabetic blood, along with the same properties of water, methylene-blue, and liquor potassæ. The mixture in each tube has a deep blue colour. Both tubes are placed in a beaker or large wide test-tube containing water. By the heat of a spirit-lamp the water in the beaker is boiled for about four minutes. At the end of this time the fluid in the tube containing the diabetic blood becomes pale yellow in colour, whilst that in the tube containing the non-diabetic blood remains blue or bluish green. It is important that the test-tubes used should be narrow, and that they should be kept quite still whilst in the water bath. The writer has invariably obtained the reaction just described in diabetes mellitus, but never in any other disease or in healthy individuals. The reaction is due to the greater reducing power of diabetic blood.

Other symptoms and complications.—The temperature is normal or subnormal except when complications occur. The skin is dry and rough in severe cases, but in mild cases it is often normal. Localised pruritus, especially about the vulva, is a common symptom. Pruritus of the vulva is often followed by erythema and eczema, and pruritus of the glans penis by balanitis and œdema of the prepuce. These complications are due to irritation caused by the saccharine urine. Boils and carbuncles sometimes develop. Gangrene, moist or dry, may occur in patients over 45. It is usually associated with arterio-sclerosis, or it follows some injury or wound of the skin. Other very rare skin affections are perforating ulcers of the foot, anasarca (without albuminuria or evidence of cardiac disease), and diabetic xanthoma. Recently a bronzing of the skin has been described in one form of the disease (*diabète bronzé*).

The mouth is usually dry and the saliva scanty. The gums are frequently inflamed and swollen, and the teeth carious in chronic cases. The tongue is often red and raw in appearance in the severe cases. Thirst is one of the most prominent symptoms, and the appetite is generally much increased; but in the mild cases both symptoms may be absent. Constipation is very common.

Tuberculous phthisis is frequent in severe forms of the disease. In

one hundred hospital diabetic patients signs of phthisis were present in twenty-nine. In elderly patients and in mild forms, phthisis is much less frequent. The phthisis of diabetic patients is nearly always tuberculous; tubercle bacilli are frequently found in the sputum; often cough and expectoration are slight; hæmoptysis is rare; and the temperature is often not much above normal. The changes found post-mortem are generally much more extensive than is suspected from the symptoms. Other lung affections are occasionally met with—chronic non-tuberculous pneumonia, gangrene, broncho- and croupous pneumonia. In severe forms of diabetes, at a late stage, the breath has often a peculiar smell, resembling chloroform, due to the presence of acetone.

The heart usually presents no signs of disease, at least in the severe forms. It was normal in ninety-three out of a hundred cases examined by the writer. Cardiac enlargement has been recorded, however, in some cases; and diabetes occasionally terminates with cardiac failure. As already mentioned, in late stages of the disease, slight albuminuria is a frequent complication (44 per cent.), but the albuminuria is usually not due to nephritis. Occasionally, however, diabetes is complicated with chronic parenchymatous or interstitial nephritis.

Defects of vision are not infrequent. Cataract, generally of the soft variety, is the most important ocular complication in 9 per cent. of cases. Vitreous opacities, paresis of accommodation, short-sightedness developing late in life, retinitis, and amblyopia are sometimes met with. Diabetic retinitis is rare, 7 per cent. of cases; it occurs only in patients over the age of 40. In one variety, small scattered punctiform retinal hæmorrhages are seen; in another variety, small "curdy" white patches, often arranged in an incomplete circle around the yellow spot, are observed near the centre of the retina. Amblyopia, like tobacco amblyopia, with central scotomata for colours, and without ophthalmoscopic changes, is sometimes met with.

Loss of sexual power is not infrequent in males; in females sexual desire is said to be diminished in severe forms, but increased in mild cases in elderly women. Amenorrhœa may occur. Abortion is common.

The intellect generally remains clear, but drowsiness, mental dulness, and melancholia are common. Troublesome cramps at night in the calf muscles are frequent, and may be the first symptom of the disease to attract the patient's attention. Tenderness of the calf muscles and pains in the legs are common; occasionally there are well-marked symptoms of peripheral neuritis, with "dropping" of the feet, as in the alcoholic form. Cases of monoplegia, probably neuritic, are also on record. When there are pains and tenderness or other neuritic symptoms in the legs, the knee-jerks are usually absent; but they are also often absent when there are none of these neuritic symptoms. Amongst one hundred hospital patients, mostly suffering from a severe form of the disease, the writer found the knee-jerks both absent in forty-nine; one present one absent in six; both present in forty-five. In private practice and amongst milder forms of the disease, the knee-jerks are much less frequently absent. At a later stage the loss of knee-jerks is more common: it was lost in 73 per cent. during the last few days of life, and in twenty out of twenty-three cases of diabetic coma. When the knee-jerks are lost, the wrist-jerks are usually also absent, but the superficial reflexes normal or increased.

Diabetic coma.—The most frequent termination of diabetes is in coma. It is especially common in severe forms of the disease in young persons.

A long railway journey, great mental worry or anxiety, great muscular exertion, sudden change of diet, and sometimes severe constipation, appear to act as exciting causes, when the patient is suffering from a severe form of the disease, and the urine gives a marked reaction with perchloride of iron. The first symptoms of this complication are rapidity of the pulse, most characteristic dyspnœa, epigastric pain, nausea, and occasional vomiting. The patient becomes restless, and then drowsiness gradually develops. The pulse becomes very feeble, and dyspnœa is one of the most prominent symptoms. The number of respirations per minute is often only slightly increased, but the inspirations and expirations are very deep, and the breathing has a peculiar sighing or panting character —the air hunger of Kussmaul. Usually the bowels are constipated; the skin is cold and livid, and the temperature subnormal, 95°–97° F. In a very few cases there is finally an elevation of temperature, 102°–104° F. The breath and the urine have usually a chloroform-like smell from acetone. The urine generally gives a distinct reaction for acetone, and a brownish red coloration is usually obtained with perchloride of iron— the diacetic acid reaction. The urine contains also β-oxybutyric acid, and the ammonia excretion is increased. The sugar excretion and the quantity of urine often diminish with the onset of comatose symptoms. The urine usually, if not invariably, contains a small quantity of albumin and a large number of granular casts in the common variety of diabetic coma. The knee-jerks are usually absent twenty out of twenty-three cases. The drowsiness steadily increases until the patient is comatose; sometimes, however, the coma is not complete, and the patient can be roused to take his medicine up to the last. Death usually occurs within forty-eight hours after the development of coma.

The symptoms just enumerated are those of the common form of diabetic coma, Kussmaul's variety; but there are two other rare forms— (1) The alcoholic forms, in which there is marked excitement at the onset, like that of alcoholic intoxication, and in which dyspnœa is not a prominent symptom. (2) Diabetic collapse, described by Dreschfeld and Frerichs; in this form there are signs of cardiac failure, followed by coma; the breath has not the acetone smell, and the urine does not give the perchloride of iron reaction.

Pathological anatomy reveals no characteristic lesions in diabetic coma; the most constant changes are those in the renal epithelium. In the variety described above as diabetic collapse, the cause is probably cardiac failure, from degeneration of the cardiac muscle.

In the common form of coma many views as to the causation have been held. Fat embolism, ptomaine poisoning from the intestine, poisoning by acetone, or diacetic acid, have, at various times and by different authors, been regarded as the cause. But there is considerable evidence against all of these views. At present there is much evidence in favour of an intoxication of the organism by some organic acid (Stadelmann), especially β-oxybutyric acid. The urine, as already mentioned, usually if not invariably, contains a small amount of albumin and numerous casts in the common form of coma; the quantity of urine and sugar excreted usually diminish; and the kidney epithelium often shows degenerative changes post-mortem. It appears probable, therefore, that in diabetic coma the kidneys fail to eliminate some toxic substances, and that poisoning is the result.

Forms of diabetic mellitus.—(1) In the mild forms removal of carbohydrates from the diet causes the sugar excretion to cease. The patients

are often past middle age, and not infrequently stout or gouty. (2) In the severe forms withdrawal of carbohydrates from the diet fails to arrest the sugar excretion; usually there is marked wasting. An acute form is sometimes met with in children and young persons, in which death occurs in a few weeks or months after the onset of the disease. (3) There are also intermediate or transitional varieties, the mild form passing into the severe. (4) In the mild forms occasionally there are no indications of the disease, except those obtained by examination of the urine—*diabetes decipiens.* (5) Occasionally in mild forms the symptoms disappear from time to time —intermittent diabetes. (6) Hanot, Chauffard, and others have described a rare form of diabetes, in which there is bronzing of the skin and hypertrophic cirrhosis of the liver—*diabète bronzé.*

Termination.—In severe forms a fatal termination occurs in a few years, occasionally in a few months. In mild cases, especially in elderly persons, the duration may be many years, ten to twenty. When nephritis occurs as a complication, the symptoms of diabetes may gradually disappear, and only those of nephritis then remain. If phthisis occurs as a complication, finally the sugar excretion and diabetic symptoms may disappear shortly before death. In a few cases diabetes mellitus has given place to diabetes insipidus.

The most frequent fatal termination is by diabetic coma—thirty-five in fifty-eight cases; pulmonary phthisis is the next most frequent termination—twelve in fifty-eight cases. Death may also occur from gangrene, carbuncle, and the various complications already mentioned.

Diagnosis and prognosis.—The diagnosis is easy. Mistakes are sometimes made because the patient complains only of wasting or of one of the complications, and the urine examination is omitted. It is important not to mistake temporary glycosuria for diabetes. If the patient be first seen in the comatose state, and the urine cannot be obtained, the reaction of the blood with methylene-blue, already described, is diagnostic.

Much depends on the patient's age and on the form of the disease. In severe forms, and in persons under middle age, the prognosis is bad. Marked wasting, the presence of the perchloride of iron reaction in the urine, and pulmonary tuberculosis, are very unfavourable signs. In mild forms of the disease in elderly people, especially in the obese or gouty, the prognosis is much more favourable; as already indicated, in such cases life may be prolonged for many years.

Treatment.—Before commencing the treatment of a case of diabetes, it is important to determine the form of the disease, as the treatment differs in the mild and severe varieties. The results obtained in the former variety are often good, whilst those in the latter are very unsatisfactory, especially in young persons. The daily amount of urine and sugar excreted should be determined, the urine should be tested with perchloride of iron, and the patient's weight noted. Then the carbohydrate articles of food should be withdrawn from the diet, and the patient should be fed on a test diet of nitrogenous and fatty food only. If the sugar excretion should be arrested by this diet, the case belongs to the mild form of the disease: a little carbohydrate in the form of bread should then be allowed, and the amount gradually increased until the glycosuria returns. The amount of bread which must be allowed before the glycosuria returns is an indication of the quantity of carbohydrates the patient can tolerate, and of the mildness or severity of the disease.

In the severe form of diabetes the withdrawal of carbohydrates from

the food does not cause the sugar excretion to cease. If the patient be wasted, and if the urine give a brownish red coloration with perchloride of iron, a rigid diet should only be continued for a very short time; and in such severe cases many authors think that this test diet should not be commenced suddenly, since by such a procedure there is a danger of exciting diabetic coma (Ebstein, Naunyn, and others). In these severe cases, if it be thought desirable to try the effect of a rigid diet, it is best commenced cautiously, potatoes being excluded first, then bread, and afterwards other carbohydrates; and it is well to allow a few days to elapse before all carbohydrates are excluded.

Having determined the form of the disease and the action of a rigid diet, the future dietetic treatment may be prescribed. A record should be kept of the sugar excretion, and of the weight of the patient. The latter is very important, and is a useful guide with respect to the diet. With the exception of cases associated with obesity, it is important to endeavour to regulate the quantity and quality of the food, so that the patient does not lose weight.

In accurate observations on the effect of diet, the amount of heat which could be produced by the oxidation of the various articles of food is often calculated and expressed in calories (a calorie being the amount of heat required to raise 1 kilo. of water 1° C.). 1 grm. of proteid and 1 grm. of carbohydrate each yield by oxidation about 4 calories, and 1 grm. of fat yields 9 calories. The quantity of these three substances in the diabetic diet is calculated, and their value expressed in calories. From the total, the value, in calories, of the sugar lost in the urine is subtracted, and the remainder ought to be not less than 2300 calories daily. This is the value in calories of the food required daily by a healthy man.

In the mild forms of the disease the test diet shows that there are two sub-varieties. In one class of cases the withdrawal of all the carbohydrates of the diet is necessary to cause the sugar excretion to cease, and the addition of the smallest amount of bread causes the sugar to return in the urine; in other cases the patient can tolerate a certain amount of carbohydrate food, and it is only necessary to restrict the carbohydrates to check the sugar excretion. In either case the diet which is just sufficient to arrest the sugar excretion should be prescribed. After a period of restriction, it is sometimes found that the patient can tolerate more and more carbohydrate food without the sugar excretion returning, and the diet may then be relaxed; but in other cases, unless the exclusion of all carbohydrate food be continued, sugar is excreted in the urine. In the latter cases, after a few weeks or months, often the patient will no longer tolerate a strictly rigid diet, or it is found that he is losing weight. It is then frequently necessary to relax the diet, especially as regards the amount of bread, and to be content if by moderate restriction of the carbohydrates we can keep the daily sugar excretion down to about 500 grs.

In the severe forms of the disease, especially when the urine gives a marked brownish red coloration with perchloride of iron, and when there is great wasting, it is now the opinion of most physicians that a very rigid diet has a bad effect. In these cases, if a strict diet be prescribed in order to test the exact form of the disease, it should only be continued for a very short time (as already mentioned). In the severe forms the diet should consist of nitrogenous and fatty food, with a small quantity of carbohydrates, chiefly in the form of bread, but all saccharine food should be avoided. Fatty food is especially valuable. Cream and butter should be given in large

quantities, and a moderate amount of milk should be allowed. If coma appears to be threatening, or if the brownish red reaction with perchloride of iron in the urine should become marked, the starchy carbohydrates in the food should be increased a little.

Articles of food in diabetes.—When it is desired to place a diabetic patient on a rigid diet in order to determine the form of the disease, or when a rigid diet is desirable in the treatment, the following articles should be sanctioned or forbidden:—

Sanctioned.—Butchers' meat of all kinds (except liver); potted and preserved meats. Ham, tongue, bacon. Poultry, game. Fish (fresh, dried, and preserved); sardines, shrimps. Broths, animal soups, and jellies (prepared without the addition of sugar or starchy materials). Eggs, cheese, cream. Butter, suet, oils, and fats. Custard (without sugar). Reliable bread substitutes (gluten bread, almond and aleuronat cakes). Green vegetables—mustard and cress, watercress, endive, lettuce, spinach, turnip-tops, cabbage, broccoli, brussels sprouts, spring onions, cucumber. Mushrooms. Pickles (cucumber, walnuts, and onions). Nuts (walnuts, almonds, filberts, hazel nuts, Brazil nuts), but not chestnuts.

Forbidden.—Sugar; saccharine and farinaceous articles of food. Pastry and farinaceous puddings. Rice, sago, arrowroot, tapioca, macaroni, vermicelli, semolina. Potatoes. Wheaten bread and biscuits. Carrots, turnips, parsnips, beetroot, beans, peas, large onions. Liver. Oysters, cockles, mussels, the "puddings" of crabs and lobsters. Honey. All sweet fruit and dried fruits.

Beverages.—*Sanctioned.*—Water, soda-water, and mineral waters. Tea, coffee. Dry sherry, claret, Burgundy, hock, Moselle, Ahr wines, most Rhine wines, Austrian and Hungarian table wines (all in moderate quantities, however). Brandy in small quantities.

Forbidden.—Port, Tokay, champagne, and sweet wines. Fruit juices and syrups. Sweet lemonade. Liqueurs, beer, ale, porter, and stout. Rum and sweetened gin. Cocoa and chocolate. Milk in large quantities.

This diet table of course requires modification according to the form of the disease, and in severe cases should be less rigid, as already indicated.

Dietetic treatment.—Nearly all kinds of animal food may be allowed, with the exception of liver, oysters, cockles, mussels, crabs, and lobsters, which contain much carbohydrate material.

Milk contains 4 per cent. of objectionable milk sugar; but it contains also a large amount of valuable fat and albumin. The glycosuria is in some cases unchanged, in others increased by milk. Cream, which contains less milk sugar, but seven times the amount of fat, may be allowed to all diabetic patients, as the total amount of sugar in the quantities which can be usually taken is very small. Milk may be allowed in the very severe cases; and also in small quantities in those mild cases in which it causes no increase of the glycosuria. The writer has prepared an artificial milk which may be taken freely by all diabetic patients: four tablespoonfuls of cream are added to a pint of water and mixed well. At the end of twelve hours the fat of the cream will have floated to the surface; it will be found almost free from sugar, which will remain dissolved in the pint of water. The cream fat on the surface of the water is skimmed off carefully, placed in another vessel, and to it are added water, the white of an egg, and a little salt, and a trace of saccharin if desired. By practice a palatable artificial milk can be thus prepared practically free from sugar. The egg albumin

may be omitted, according to the patient's preference. Fats of all kinds are of great value, especially in the form of butter, cream, bacon, cheese, eggs, suet, and cod-liver oil. A little brandy and water aids the digestion of these articles.

As regards the various carbohydrates, starch is less injurious than sugar. Fruit sugar (levulose) is less injurious than cane sugar and grape sugar. In mild forms a small amount of fruit sugar is utilised in the system. Fruits which contain much sugar, such as grapes and dried fruit, dates, figs, raisins, currants, etc., should be forbidden; but some fruits contain only a very little sugar, which is chiefly in the form of lævulose, and a *very small* quantity of such fruit is sometimes allowed when a very rigid diet is not necessary. Saccharin or saxin should be used in place of sugar to sweeten tea, coffee, and articles of food.

Bread contains 49 per cent. of carbohydrates, and 2 per cent. of sugar, and on this account is objectionable when a very rigid diet is indicated; but its substitutes are often unreliable owing to their disagreeable taste, or on account of the large percentage of carbohydrates they contain. When a very rigid diet is not indicated, it is best to allow a small quantity of ordinary white bread; but if for diagnosis or treatment a strict diet is desired, a reliable bread substitute may be given for a time. The following are the most useful bread substitutes:—(1) Gluten bread, which ought to contain only a very small amount of starch; but many preparations contain much starch, and therefore a rough test with iodine is necessary before recommending any specimen. (2) Soya biscuit and bread, prepared from the soya-bean. The taste is often objectionable, however, and the preparations not infrequently contain a large amount of starch. (3) Almond cakes. Four oz. of almond flour are mixed with a little water and German yeast. The mixture is allowed to stand in a warm place for twenty minutes, then an egg beaten up, and a little cream and water are added and a paste formed, which is divided into cakes and baked for fifteen to thirty minutes. (4) Cocoa-nut cakes. They are prepared in the same way as the almond cakes, desiccated cocoa-nut powder being used in place of almond flour. Both almond and cocoa-nut cakes contain much fat, and a little alcohol aids their digestion. (5) Aleuronat. This is a vegetable albumin recommended by Ebstein, which contains only a very small amount of carbohydrates. The writer has found that palatable and reliable cakes can be prepared as follows:—Two oz. of desiccated cocoa-nut powder are mixed into a paste with water and German yeast. The mixture is kept in a warm place for twenty minutes, then two oz. of aleuronat, one egg (beaten up), water, and a little solution of saccharin are added. The whole is well mixed, divided into cakes, and baked.

Beverages free or almost free from carbohydrates may be allowed. A little alcohol is of service in aiding the digestion of large quantities of fatty food, but only those forms should be allowed which contain little or no carbohydrates. Diluted acid drinks are of service in relieving the thirst. A lemonade may be made of a little citric acid and glycerin in a pint of water.

The patient should be relieved of mental anxiety and worry as much as possible. In mild forms in stout individuals, vigorous exercise in the open air is of service, but in the severe form it is injurious.

Certain continental spas—Carlsbad, Marienbad, Neuenahr, Vichy—are much frequented by diabetic patients. In the mild forms of the disease, especially in stout or gouty persons, often benefit is derived from a visit to

these spas; but in the severe forms tne long journey is most injurious, and the waters are useless.

Medicinal treatment.—We have no drug remedy for the disease in its severe form; but several drugs have been shown to have some good effect, especially in the milder forms. Opium, morphine, and codeine are of service in many cases. The doses may be steadily increased (from ½ gr. of opium up to 2 or 3 grs.) three times a day; and from ½ gr. of codeia up to 2 or 3 grs.). These preparations are best given after a meal; but they are liable to give rise to severe constipation.

Alkaline salts—bicarbonate of soda, citrate and acetate of potash, etc.—have been long used. Naunyn strongly advocates very large quantities of sodium bicarbonate (150 to 250 grs. daily) in the severe forms of the disease, when there is a marked reaction in the urine with perchloride of iron, or when coma appears to be threatening.

The following drugs amongst many others have oeen also recommended:—Arsenic (in mild cases), jambul in large doses, sodium salicylate, bismuth salicylate, uranium nitrate, lithium salts (especially in cases associated with gout). Probably in mild cases, these drugs, when pushed, do have a beneficial effect. In mild forms the writer has obtained very marked reduction of the sugar excretion, along with general improvement, by the use of sodium salicylate (15 or 20 grs. four or five times a day). Cod-liver oil is of service when the patient is much wasted.

Treatment of complications.—For the prevention or alleviation of irritation or eczema of the vulva or prepuce, it is important to dry the urethral orifice with lint or absorbent wool after micturition. When the affections mentioned have developed, the application of boracic acid ointment or lotion is of service. The treatment of other complications will be found in the various articles devoted to these subjects.

Prevention and treatment of diabetic coma.—In the severe form of the disease there is always a danger of coma developing, especially when there is great wasting and when the urine gives a marked reaction with perchloride of iron. In such cases, over-exertion, long railway journeys, sudden change of diet, are dangerous, and constipation should be avoided. When coma appears threatening, the diet should not be rigid. Cream, milk, and fatty food should be given freely, and a small amount of carbohydrates (chiefly bread) should be allowed. Schmitz believed that early coma could be often checked by purgation with castor-oil. When the early symptoms of coma appear, large doses of alkalies should be given at once (100–400 grs. of bicarbonate of soda in the twenty-four hours). It may be given in milk in frequent doses, or as an effervescing mixture with citric acid; or sodium citrate may be given in solution in large doses (Lépine).

During the last ten years intravenous injections of alkaline solution, as suggested by Stadelmann, have been often employed. The solutions most frequently used have been a 3–5 per cent. solution of sodium bicarbonate in water, or in 0·6 per cent. sodium chloride solution; often a solution of sodium chloride alone has been employed. The solution should be warm when used (100° F.). It is usually injected into the median basilic vein of the arm. Two or three pints should be injected. Frequently its only effect is to improve the pulse and to slightly diminish the coma. Occasionally the patient regains consciousness for a short time, so that he can converse with his friends, but a relapse soon occurs. Intravenous injections may be of service, therefore, if the patient has not seen his friends for a long time. Lépine strongly advocates alkaline intravenous injections *before*

actual coma has devoloped, and directly the first symptom of the commencement of this complication appears. He thinks that it is only at this stage that we can hope for permanent good results.

R. T. WILLIAMSON.

DIABETES INSIPIDUS.

DIABETES INSIPIDUS is characterised by great thirst, and persistent excretion of very large quantities of urine free from sugar and albumin. The disease is sometimes secondary to localised organic disease of the brain ; but in most cases there is no evidence of any other associated affection.

Etiology.—The disease is very rare. At the Manchester Royal Infirmary, during a period of ten years (1888–1898), amongst 14,575 medical in-patients, there were only seven cases of diabetes insipidus. Males are affected about twice as frequently as females. The disease may occur at almost any age, but Ralfe has shown that it is most frequently met with in early childhood (1–10 years), and in early middle age (30–40). A number of instances are on record in which there has been a family history of the disease—brothers, sisters, or parents having been affected. Occasionally there is a family history of diabetes mellitus or gout, and frequently of tuberculosis.

The disease has been attributed in some cases to injuries to the head, to worry and anxiety, fright, great mental excitement, malnutrition and neglect, alcoholism, influenza, and other acute affections, syphilis, and exposure to cold. A good number of cases have been shown, by post-mortem examination, to be due to cerebral disease. Often no exciting or predisposing cause can be traced.

Pathology.—There are no characteristic morbid anatomical lesions in diabetes insipidus. Often changes of various kinds have been found in the portions of the brain situated in the posterior fossa of the skull (medulla, pons, cerebral peduncles, cerebellum). In these cases diabetes insipidus has formed a part of the symptomatology of the brain affections. In the primary or idiopathic cases an autopsy is seldom obtained, and the reports published have often been incomplete, or the changes observed have been unimportant. Hypertrophy of the kidneys and dilatation of the renal vessels have been often observed, but these changes are probably secondary.

Pathogenesis.—Temporary polyuria (without glycosuria) was produced by Claude Bernard, by puncture of the floor of the fourth ventricle a little above the so-called "diabetic centre." Eckhard has shown that section of the great splanchnic nerve produces increased urinary excretion from the kidney on the side of the experiment. Kahler produced permanent polyuria by lesion of the side of the posterior part of the pons and anterior part of the medulla.

Diabetes insipidus in man is regarded by many as due to a disturbance of the function of the kidneys—a renal neurosis owing to vasomotor disturbance of the renal blood vessels. In some cases, this disturbance is secondary to a lesion of cerebral structures in the posterior fossa of the skull, as already mentioned : possibly in a few cases lesion of the splanchnic nerves may be the starting-point of the affection. In rare cases, apparently the symptoms are due to hysteria, the diuresis being the result of drinking large quantities of fluid.

Symptoms.—The two prominent symptoms of the disease are thirst and diuresis, and the onset may be insidious or sudden. The amount of urine is very great—greater than in any other disease: it varies from 180 to 400 or 500 oz. daily. The total solids are usually normal in amount, but the percentage is much diminished. The urine is clear, very pale with a faint yellow tint—like water to which a few drops of urine have been added. The reaction is slightly acid. The specific gravity is very low, under 1010; usually it is from 1002 to 1004; sometimes 1000·5 or 1001. The quantity of urine is greater than the amount of fluids drunk, but only a little greater than the total amount of water in the liquids and solid food taken. Often the night urine is more abundant than the day urine; sometimes the excretion in the two periods is equal.

Albumin is absent: in the few cases in which it has been found, probably some complication has been present. Glucose also is absent. Not infrequently inosite has been detected, but it is not important: in many cases it is absent, and in healthy persons it is sometimes found in the urine after a large quantity of water has been taken. The total excretion of urea is usually normal; but in some cases it is increased, in others diminished. The excretion of uric acid and kreatine is usually normal. Sodium chloride is sometimes increased, sometimes diminished: the sulphates and phosphates are usually normal. Teissner has recorded cases in which the excretion of urine and the amount of phosphates have both been increased, and to these he has given the name of phosphatic diabetes. Some cases occur spontaneously; others are associated with phthisis.

Thirst is the second prominent symptom; it is excessive, and the mouth and tongue are dry. The skin is usually dry and the sweat diminished. The appetite is often unaltered; in some cases it is increased; in others diminished. Constipation is a common symptom. The general condition in some cases is not altered, and the health is good apart from the thirst and diuresis; in other cases there is progressive wasting. There is no cardiac hypertrophy. Cataract has been observed in a few cases. Hemianopsia has been occasionally recorded. The temperature is usually subnormal. In most cases restriction of the quantity of fluids taken can only be tolerated for a few hours or days; but a few cases are on record in which the symptoms ceased, or very markedly diminished, when the fluids were greatly restricted for a time. The amount of urine is diminished by intercurrent febrile affections.

Forms of the disease.[1]—(1) Many cases are on record in which diabetes insipidus has been associated with chronic brain diseases, chiefly tumour, tubercle, gumma, cysticercus, etc., in the floor of the fourth verticle; sometimes there has been a lesion in the medulla, pons, or cerebral peduncle, and occasionally in the cerebellum; occasionally the cerebrum has been affected (softening of the basal ganglia and cortex). The symptoms of diabetes insipidus may develop along with the cerebral symptoms, or they may precede or follow the onset of the latter. The amount of urine in such cases is usually about 140 to 200 oz., and the polyuria continues until the death of the patient, or ceases only a few days before death. (2) Diabetes insipidus following head injuries is a more common form. The polyuria is moderate in amount: it may disappear in a few weeks or years, or it may continue for many years up to the end of life. (3) In another form the disease is associated with hysteria or epilepsy. The amount of urine is usually about 100 to 180 oz. (4) In some cases there is no

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[1] This classification is slightly modified after D. Gerhardt.

evidence of hysteria, but the sudden onset after fright, and the sudden disappearance of the symptoms, appear to point to a functional cerebral affection. (5) In the idiopathic cases no primary disease can be detected; the symptoms are marked for a time, and there is wasting and weakness: then improvement often occurs, and apart from the thirst and diuresis the patient feels well. In this group of cases the amount of urine is enormous. The duration of the disease is very long, and a post-mortem examination is seldom obtained. (6) Cases in which the disease is hereditary have a similar course to the idiopathic cases. (7) Occasionally cases of diabetes insipidus are associated with syphilitic disease of the brain, or they occur in syphilitic individuals, and improve under antisyphilitic treatment.

Diagnosis and prognosis.—The low specific gravity and the absence of sugar distinguish the cases from diabetes mellitus. The absence of albumin and cardio-vascular changes separate them from the various forms of Bright's disease. The persistence of the diuresis excludes temporary polyuria, which sometimes occurs in connection with various diseases.

The prognosis varies according to the form of the disease. In a few rare cases complete or partial recovery has been reported; some cases soon terminate fatally, especially those associated with gross cerebral lesions; whilst in other cases the symptoms may persist for many years without much impairment of health, and if death occur it is owing to some accidental complication. In one of the writer's cases diabetes insipidus has been present for six years. At first wasting and other symptoms were well marked, but for several years there has been great improvement; thirst and diuresis are now the only symptoms which trouble the patient; she is well nourished, is able to do heavy work, and feels in good health.

Treatment.—If any disease be present to which diabetes insipidus is secondary, the treatment should be directed to the primary affection.

In the majority of cases restriction of fluids has no curative effect, and it cannot be long tolerated. In a very few cases, however, restriction of the amount of fluids is followed by great improvement or recovery: such patients have usually been hysterical, but in others there has been no evidence of hysteria, and the condition has been then regarded as the result of the habit of taking too much fluid (D. Gerhardt).

Galvanism has been followed by remarkable improvement in a few cases, whatever the exact explanation may be. One large electrode (positive) has been placed at the back of the neck, and the other (negative) on the epigastrium or chin, or by means of an insulated electrode, on the posterior wall of the naso-pharynx. The strength of the current should be 1–5 mille-ampères, and the duration of the application about five minutes. Valerian was recommended by Trousseau in large doses, but it frequently causes much nausea. Valerianate of zinc and antipyrine have been occasionally followed by considerable improvement. Ergot has been found to diminish the amount of urine, but its continued use is liable to give rise to ergotism. Ralfe has shown that nitro-glycerin may sometimes cause marked improvement. Warm clothing is important, in order to increase the action of the skin. Ice and acid drinks are of service in relieving thirst. As regards food, restriction of the carbohydrates is not necessary in diabetes insipidus, and a mixed diet may be taken. It is advisable to take very little salt with food.

R. T. WILLIAMSON.

SUNSTROKE.

Syn., Heatstroke, Thermic Fever, Siriasis.

SYNCOPAL, pyrexial, and hyperpyrexial conditions occurring in high atmospheric temperatures, or as a consequence of exposure to the direct rays of the sun.

History and geographical distribution.—The dangers of exposure to the direct rays of a powerful sun have always been recognised, but the recognition of the relationship of the condition known as "thermic fever" to sun exposure and high atmospheric temperatures is comparatively recent, and is due principally to our army medical officers in India and to American writers.

Although occurring at times in temperate climates during the summer and autumn seasons in the harvest field, and, more especially, in crowded cities, these affections are most commonly met with in the tropics, more particularly in low-lying, damp, malarious localities, and where the atmosphere is still and saturated with watery vapour. Compared to the coast lands, the dry uplands are comparatively exempt, notwithstanding the high temperatures that are frequently encountered there. Thermic fever becomes epidemic at times over small, occasionally over very large, areas. Stokers, and even passengers in steamers passing through the tropics, are not infrequently attacked both by syncopal sunstroke and by thermic fever; the Red Sea, from June to November, has a deservedly evil reputation in this respect. The workmen in sugar factories and similar industries associated with prolonged exposure to high temperatures, are subject, even in temperate climates, to syncopal attacks from over-heating at their work.

Etiology.—Confining the expressions heatstroke and sunstroke to the sudden collapse which occurs during, and manifestly in consequence of exposure to high atmospheric temperatures, or to the direct rays of the sun, investigation of individual cases has demonstrated that, whilst a few healthy individuals may suffer in this way, the majority of cases occur in exhausted or unhealthy individuals, and are really examples of simple syncope or exhaustion. They are found among those who are worn out by sustained muscular effort, especially when the patient is over-burdened with thick clothing, among those labouring under the effects of excess in alcohol or food, or who are the victims of malaria, of heart, kidney, or other organic or constitutional disease. All over-strain, excess, and disease, therefore, powerfully predispose to syncopal sunstroke or heat exhaustion.

The same remark applies to thermic fever or heat apoplexy, as it is sometimes called. As in the syncopal type, so in this form of thermic disease, the direct action of the sun's rays, although often powerfully contributory, is not necessary to call forth the symptoms. An over-heated, still, impure, steamy atmosphere, such as is often found in overcrowded barracks, or in troopships, together with intemperance, are perhaps the commonest of the predisposing etiological elements; but the nature of the premonitory phenomena in many of these attacks, the facts of geographical distribution, and the peculiarities of endemic and epidemic occurrence, seem to indicate that simple heat or overcrowding, even if combined with excess, are not the only factors in every form of thermic fever.

Many of these thermic fevers or heat apoplexies may be purely the consequence of heat, and the result of an overthrow of the thermal dynamics of the body by heat in those who are physiologically unsound. Many I

believe to be pernicious malarial attacks. Possibly, as suggested by Sambon, others are the effects of an as yet unknown specific germ, which finds its necessary extracorporeal conditions only in the presence of high atmospheric temperature. These thermic fevers, like many other tropical fevers, have yet to be studied in the light of a possible relationship to the plasmodium of malaria and to other germs.

Race and habituation have a very manifest influence on susceptibility. The European, especially the new-comer in the tropics, is much more liable to heatstroke and thermic fever than the native and the acclimatised European. Women and children suffer less than men, probably because they are less exposed to the sun and are more temperate.

Morbid anatomy and pathology.—If the body be opened directly after death from thermic fever, the left heart is found firmly contracted, the right heart dilated and, along with the pulmonary arteries and venous system generally, gorged with blood. Death manifestly takes place from asphyxia. Post-mortem rigidity sets in very early, and decomposition is rapid. In cases that have survived for some time, evidences of chronic meningitis may be discovered.

Many theories have been propounded as to the pathology of thermic fever. The general belief is that the symptoms in the first instance are due to a breakdown and consequent inadequacy of the heat-lowering mechanism of the body, in the presence of a high atmospheric temperature. Subsequently, and when, in consequence of this, the body temperature attains 108°, or over, there is liability to coagulation of myosin and destruction of the contractility of all muscular organs, including the heart. Wood points out that in muscular tissue exhausted by recent and sustained effort, the myosin coagulates at a lower temperature than when the muscles are at rest and not exhausted; hence, he says, those rapid deaths from sunstroke which sometimes occur in soldiers during the excitement of battle in a hot climate. Parkes cites the case of the 19th Regiment in the first Chinese War. The soldiers fought on a very hot day, and in heavy and unsuitable clothing. Many cases of sunstroke occurred; in these in every instance the men fell forward on their faces suddenly, as if struck by lightning, and died immediately. Wood interprets this as sudden coagulation of myosin by a high temperature acting on an exhausted, overstrained heart muscle.

Symptoms.—*Apyretic type.*—It would appear that there are two forms of the apyretic type of sunstroke—the syncopal and the algid. In the former there are feelings of faintness which may or may not culminate in syncope; it occasionally proves fatal. In the latter, in addition to the syncopal condition, there are marked nervous symptoms, accompanied, perhaps, by delirium or by unconsciousness, the pulse being feeble and irregular, and the temperature subnormal—95° or 96°; profuse sweating is usually a prominent symptom, and death is not uncommon.

Thermic fever.—During exposure to high temperature, especially if prolonged and in the presence of the predisposing conditions already referred to, thermic fever, or, as it is sometimes called, heat-apoplexy, heat-asphyxia, or siriasis may supervene. The more definite symptoms are sometimes preceded for a few hours or days by feelings of intense languor, by vertigo, præcordial distress, mental confusion, thirst, frequency of micturition; in other instances the disease shows itself quite suddenly, the patient lapsing almost instantaneously into a condition of profound unconsciousness. For a short time, a few minutes only it may be, the

coma may be preceded by delirium. Very often there is no warning of this description, the attack coming on during the night, perhaps, and apparently during sleep. When the attack has fully developed, the breathing may be rapid and shallow, or it may be deep and stertorous. The face is sometimes flushed, sometimes cyanosed, sometimes pale; the conjunctivæ are injected; the pupils are contracted, dilated, or normal; the skin is intensely hot, and either exceedingly dry or profusely perspiring. The temperature of the body mounts rapidly to anywhere between 108° and 112°. There may be subsultus, great restlessness, perhaps convulsions. Very soon, if not relieved, in the course sometimes of half an hour or at most a few hours, the pulse becomes exceedingly rapid, flutters, and finally fails, and the patient dies.

Recovery under favourable conditions from minor degrees of thermic fever may occur; but for the most part convalescence is slow, the patient suffering much from headache, pains in the neck, vertigo, mental debility, and sometimes from insanity. For a long time he is exceedingly sensitive to exposure to the sun, and even to warm and especially overcrowded rooms; he gets headache at once under such circumstances. Ultimately he may recover entirely, but very often a condition of permanent invalidism is established. What used to be known as ardent fever may, in some instances, be a mild variety of this form of sunstroke.

Diagnosis.—The conditions under which thermic fever occurs are a principal guide in diagnosis. Insensibility and high temperature in hot weather are generally held to mean thermic fever or heat apoplexy. That this diagnosis is always correct is at least doubtful. As already stated, many of these are probably cases of pernicious malarial fevers; the microscope, therefore, should always be used to settle this point—so important in directing treatment. Ordinary apoplexy may be followed by high body temperature; but the sequence of events in this case is the opposite to that occurring in thermic fever, in which high body temperature precedes the insensibility.

Treatment.—In syncopal sunstroke the indications are to rest the body, to get blood to the brain, and to stimulate the heart. The patient should be taken out of the sun into a cool place, laid flat on his back, and fanned gently; his clothes and accoutrements being unloosed, whisky, or ether, or ammonia should be administered, and the patient otherwise treated as for ordinary fainting. If the body temperature is below normal, a warm bath or rectal injection of very hot water, as well as diffusible stimulants, are indicated.

In thermic fever the patient should be placed in water at a temperature of 80° or 85° F., and the water gradually cooled down by means of ice. The duration of the immersion must be regulated by the effect on the thermometer kept in the rectum. Where the bath is not possible, as on the line of march, the patient should be immediately carried into the shade, his clothing removed, and the body freely and frequently soused with cold water. Rubbing with ice, when this can be got, and enemata of iced water are valuable accessories. Care must be exercised not to push the cold bath too far, or to depress a failing heart by sudden shock. It is well to remove the patient from the bath when the temperature has sunk to 101° F., for it must be kept in mind that body temperature may continue to fall to a dangerously low point, even after removal from the bath. Although temperature be reduced to normal,

insensibility may persist; the prognosis is then very unfavourable. Sometimes a large blister applied to the scalp is of service in these circumstances. In all cases in which malaria is possible, particularly if the plasmodium be discovered in the blood, hypodermic injections of full doses of quinine must be immediately employed and repeated (see "Malaria"). Any tendency to recurrence of high temperature must be met immediately by recourse to the cold bath or cold affusion. Respiration failing whilst the heart's action continues suggests the persevering employment of artificial respiration, combined with efforts to reduce temperature; lives have been saved in this way.

For the chronic meningitis, so apt to follow in these cases, iodide of potassium, small doses of mercury, frequent blistering of scalp and neck, mild purging, rest, a cold climate, light diet, and avoidance of all stimulants and excitement, are the best measures.

Prophylaxis. — Strict temperance in eating and drinking, care about exposure to the sun, the use of pith helmets and white umbrellas, light and open clothing, free ventilation, abundant cubic space in barracks and on board ship, an abundant supply of drinking water, are the best prophylactics. Those who have once suffered from sunstroke or thermic fever, or conditions approaching these, are unsuited for the Tropics.

PATRICK MANSON.

AFRICAN LETHARGY.

Syn., Sleeping Sickness.

A DISEASE of the nervous system endemic in and limited to West tropical Africa, and characterised by a gradually increasing lethargy and somnolence. It runs a slow course of months or years, and is probably invariably fatal.

History and geographical distribution.—This disease has been known for about a century; we are still in the dark, however, as to its cause and pathology. It is endemic, and, as far as known, absolutely confined to West tropical Africa, being found here and there throughout the basins of the Senegal, the Niger, and the Congo. Its distribution is singularly capricious: some districts are absolutely free from the disease, whilst in others it is so prevalent at times as almost to decimate the population. Although sleeping sickness can be acquired only within the endemic area, its manifestation may not take place until many years after the endemic area has been quitted. Thus a negro may leave West Africa in perfect health, and remain so for many years, and yet at the end of this time he may develop sleeping sickness and die of the disease in some foreign land.

Etiology.—Age, sex, and occupation seem to make no difference in the liability to this disease. Several cases may occur in the same house, men, women, and children being indiscriminately attacked. Hitherto the negro has almost exclusively been affected. We may not conclude from this, however, that there is any special racial susceptibility, but only that there is special opportunity in the case of the negro.

The cause of the disease has been a subject of much speculation; amongst other things manioc-eating, intemperance of all descriptions,

exposure to the sun, malaria, and so forth, have been impugned. Investigation, however, shows that these have nothing to do with it.

Some time ago the writer pointed out that the negro in West tropical Africa frequently harbours a peculiar blood worm, *Filaria perstans*. From the circumstances that the geographical distribution of this parasite[1] and that of sleeping sickness are singularly limited, and that their geographical areas correspond ; and, furthermore, because the parasite may live in the blood of its host for many years after the endemic area has been quitted, and that manifestations of sleeping sickness may not occur until years after the negro has left his home, there seems to be some probability of a connection between this parasite and the disease. The writer has suggested that, considering the habits of similar parasites, and the nature of the symptoms produced by them, it is possible that *F. perstans*, by interfering in some way with the nutrition of the brain, may bring about sleeping sickness.

Pathology.—There is no coarse lesion of the brain. In two post-mortem examinations of negroes with this disease, recently made by Mott, abundant microscopical evidence, in the form of small-cell infiltration of the perivascular spaces of a meningo-encephalitis, was discovered.

Symptoms.—Sleeping sickness begins very insidiously. A gradually increasing torpor and physical languor, together with occasional attacks of headache, vertigo, and fever, and a peculiar apathetic, sleepy expression of the face, herald the oncoming of the disease. By degrees the lethargy becomes so pronounced that the patient ceases to attend to his work, and lies about asleep, or half-asleep, in the corner of his house. After a time this condition becomes more pronounced, so much so that he will no longer feed himself. Nutrition begins to suffer, bedsores may form, and additional nervous symptoms, such as tremor, convulsive movements, and temporary paralyses may supervene. The soporose condition becomes more intense, and gradually the patient succumbs from asthenia, or perhaps may die in a convulsive seizure. During the progress of the disease, maniacal symptoms, conditions resembling those in general paralysis of the insane, an ataxic drunken gait, and so forth, may develop, and come and go. The skin of the patient is harsh, dry, and furfuraceous, and is often affected with an exceedingly irritable papular or vesicular eruption. The lymphatic glands of the neck and elsewhere are generally swollen. Sleeping sickness may prove fatal in four or five months, or it may last for as many years. A year to eighteen months is perhaps the average duration.

Diagnosis.—By some this disease has been confounded with beriberi. There is no difficulty, however, in diagnosis. The symptoms of beriberi are those of a peripheral neuritis with special liability to implication of the pneumogastric nerves, to œdema, to dilatation of the heart, and palpitations. Sleeping sickness, on the other hand, is manifestly a disease of the central nervous system, and characterised by torpor, tremor, and, in the advanced stages, convulsive seizures—phenomena practically unknown in beriberi.

Treatment.—No treatment, so far as known, is of any permanent service.

<div align="right">PATRICK MANSON.</div>

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[1] Quite recently I have found this blood-worm in Demerara Indians. There is no reliable information obtainable as to the presence or absence of sleeping sickness among these people.

SECTION II.

DISEASES CAUSED BY ANIMAL PARASITES.

———

PROTOZOA.

RHIZOPODA.

AMŒBA COLI.—This protozoon, discovered by Lösch in 1875, is by no means the only amœba frequenting the alimentary canal of man. The other amœbæ, however, have, so far as known, no special pathological bearing. Amœba coli, on account of its size, the activity of its movements, the ease with which it can be demonstrated, and especially on account of its frequent association with dysentery and liver abscess, apparently deserves the considerable amount of attention which of late years it has received.

It resembles in appearance and movement the ordinary freshwater amœba. At first sight it looks like a minute piece of clear, structureless jelly, spherical when at rest, irregular in form, with rounded pseudopodia (which it keeps constantly pushing out and creeping after), when in a state of activity. Under a magnifying power of 200 to 300 diameters, it is seen to consist of a clear, pellucid outer layer—"ectosarc" —of which the pseudopodia are mainly constituted, and a somewhat granular greyish central portion—the "endosarc." The latter contains an ill-defined nucleus and nucleolus, one or two vacuoles, and, very likely, bacteria, blood corpuscles, and débris of different sorts which it has included. In a state of repose the amœba measures from 15 μ to 20 μ

FIG. 48.—*Amœba coli.* (a) *A. dysenteriæ* fixed and stained.—Councilman. (b) *A. dysenteriæ* in stools.—After Lösch.

in diameter; roughly speaking, its diameter is equal to about that of from three to five blood corpuscles.

Amœba coli occurs in the healthy fæces both of man and of certain lower animals. It is very frequently, though by no means always, present in the stools in dysentery. In these, when present, it can be readily demonstrated. All that is necessary is to compress between cover-glass and slip, so as to form a thin translucent layer, a fragment of mucus from the fresh stool; search is then made with a magnifying power of 100 to 200 diameters. In some cases of dysentery the parasite is present in great abundance, and many specimens may be seen in every field; usually, however, several fields have to be scrutinised before a specimen is discovered. When the temperature of the slide falls below 70° F., the amœba assumes its passive form; even in this condition, with a little experience, it may be recognised by its size, spherical form, slightly greenish pellucid tint, and sharp outline. When the temperature of the slide is raised, in many specimens, though not in all, the characteristic amœboid movements set in, becoming more active as blood heat is approached. In this climate, therefore, in making a microscopical examination, some form of warm stage is desirable. The amœboid movements may continue for several hours; they cease at once on the temperature being allowed to fall. In most slides a proportion of the amœbæ maintain their pellucid, spherical, and probably encysted form, even if the temperature be raised.

In liver abscess, the amœbæ, when present, are readily found in the pus, especially in the pus escaping from the drainage tube several days after the abscess has been opened surgically; they continue present so long as the chocolate-coloured pus, characteristic of liver abscess, is being discharged, and even in the yellow pus coming from the healing abscess cavity or sinus. I have frequently found the amœba in the pus coming from the drainage tube in cases in which several days before I had failed to discover it in the pus coming from the abscess at the time of operation; that is to say, the special habitat of the amœba is the wall of the abscess and the pus in immediate contact with this. It has been found in the pus coughed up from liver abscess discharging through the lungs; its presence, therefore, is a valuable diagnostic sign of this condition.

Amœbæ are sometimes demonstrable in the tissues forming the base of certain dysenteric ulcers, as well as in the disintegrating hepatic tissue constituting the wall of a liver abscess.

There is by no means unanimity among pathologists as to the significance of this parasite; some maintain that it is the cause of a certain type of dysentery; others, that in such cases it is merely a concomitant. Its bearing on liver abscess is equally obscure. (See " Dysentery " and " Liver Abscess.")

Treatment.—The amœba is very sensitive to quinine; it may be made to disappear, at all events temporarily, from the discharges, by injections of weak solutions of the drug—1 in 2000—whether into the colon or into the cavity of a liver abscess. Although Lafleur regards its presence as, prognostically, very unfavourable, I have seen many liver abscesses in which amœbæ abounded recover perfectly after operation. I therefore do not regard it as an important factor in prognosis.

GREGARINIDÆ.

COCCIDIUM.—Several species of coccidia have been found in man. Our knowledge of the subject, however, is extremely fragmentary. For the

present its principal interest is an analogical one, and lies in the light it tends to throw on the life history of the malaria parasite, and possibly on the etiology of malignant and certain other growths.

The *Coccidium oviforme*, which is more especially a parasite of the rabbit, but which has also been found in man, may be regarded as a type species. Like all coccidia, it is an intracellular parasite. It inhabits the epithelium of the bile passages and of the intestine. Introduced in its encysted form (Fig. 49) with the food, the coverings are dissolved by the digestive fluids, and the eight falciform sporozoids which it contains are set free. These then probably acquire amœboid properties, and work their way along the bile ducts, or intestinal canal, finally penetrating the epithelial cells, where they grow at the expense of the protoplasm of the cell, at the same time thrusting the nucleus to one side. Recent researches (Pfeiffer, Simond, Leger) make it probable that at this and subsequent stages the young parasite may follow one or other of two directions in development; one securing the multiplication of the organism within the host, the other directed to secure the passage of the parasite from one host to another.

In the former case (endogenous or *eimeria* form), after attaining a certain size, the little organism divides into a number of segments, each of which, on the bursting of the including epithelial cell, breaks away, and,
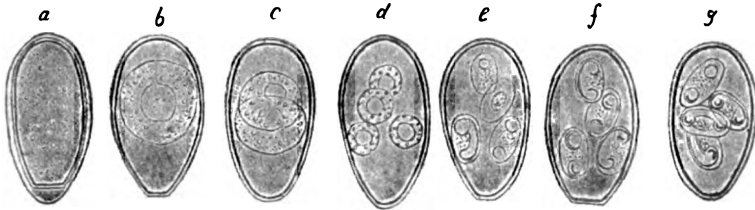
Fig. 49.—*Coccidium oviforme*, from the liver of the rabbit. (× 550.) *c-g*, stages of spore-formation only observed in the free state.—Leuckart.

moving actively—possibly as a flagellated sporozoid—enters another epithelial cell, and repeats the cycle. In the second event (coccidial or exogenous form), and probably as an ultimate event after a series of eimeria generations, when the parasite has attained a size of from 25μ to 30μ, it becomes encysted, and, continuing to grow, assumes an ovoid form (40μ to 50μ by 21μ to 28μ) (*a*). The granular protoplasm now contracts, and a clear central zone, suggestive of a nucleus, is formed (*b*). The coccidium then escapes from the epithelial cell, and, falling into the bile ducts or intestine, is carried out of the body of the host with the fæces. Development continues to progress; the protoplasm divides into two, then into four (*c*, *d*) spherical sporoblasts, which, assuming an oval form, acquire a membranous covering (spores). Finally, the protoplasm of each of these spores divides into two nucleated falciform bodies and a residual body (*e*, *f*, *g*). This the extracorporeal phase is now complete, and becomes infective on being transferred to the stomach of an appropriate mammalian host.

In the rabbit, aggregations of these parasites form whitish tumours, the size of small nuts, in the liver, each tumour including enormous numbers of coccidia at all stages of development. Grave secondary changes ensue, ending in dilatation of the bile ducts, proliferation of the connective tissue, and atrophy of the liver cells. Ultimately the animal suffers from diarrhœa, and, becoming extremely anæmic and wasted, dies in convulsions. On

dissection, the liver is found enlarged and stuffed with coccidial growths, the intestinal mucosa being eroded with disseminated coccidial ulcerations.

SARCOSPORIDIA. — Certain bodies, variously known as *Sarcosporidia*, psorosperm sacs, and, when occurring in the muscles, as Miescher's tubes
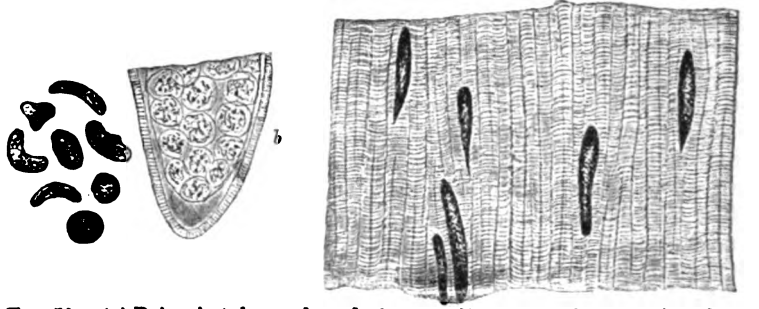
FIG. 50.—(*a*) Rainey's tubes, enlarged about 40 diameters ; (*b*) extremity of one of Miescher's tubes, with its contents. At the side are the kidney-shaped bodies, much enlarged.—Leuckart.

or Rainey's bodies, are frequently present in the tissues of the pig, rat, mouse, deer, and other animals, and occasionally in those of man (Fig. 50). The natural history and significance of these bodies have not been made out. Several species have been described. They consist essentially of an external cyst enclosing a vast number of extremely minute falciform, oval or spherical bodies, arranged in groups more or less distinct (Fig. 50). In the muscles, a favourite situation, they may attain a considerable length—1 mm. to 2 mm. by 77 μ to 168 μ ; they occupy the interior of the fibres. Elsewhere, in the intestine, connective tissue, heart, kidney, and liver, they are generally oval or round, and may measure from 20 μ to 30 μ up to 350 μ in diameter. Kartulis has recorded a case in which bodies of this description gave rise to fatal abscess of the liver.
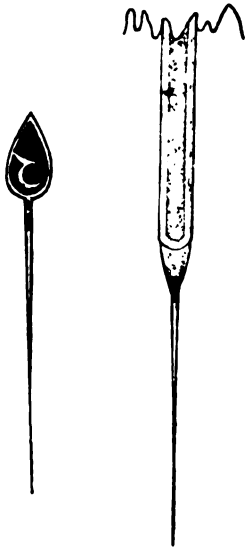
INFUSORIA.

MONAS PYOPHILA.—A flagellate organism, discovered by Grimm in the pus expectorated from a liver abscess in a Japanese, which had ruptured through the lung. It resembles a gigantic spermatozoid, 30 μ to 60 μ in length. In the case in question the parasite was present in great abundance.

FIG. 51.—*Monas pyophila.*

PLAGIOMONAS IRREGULARIS, also belonging to the flagellata, is a pyriform body, 10 μ to 15 μ in length, carrying two flagella on its larger rounded end. It was found by Salisbury in the United States, and by Kunstler at Bordeaux. In both instances it was found in the urine.

TRICHOMONAS VAGINALIS is also a somewhat similar pyriform organism, 10 μ to 15 μ by 7 μ to 10 μ, with a very plastic body carrying

four flagella springing from one point on its larger and rounded extremity. From the same point an undulating membrane runs backwards to the other, or posterior pointed and occasionally elongated extremity. A funnel-shaped mouth opens near the base of the flagella. It reproduces by longitudinal division. It occurs in unhealthy, particularly acid, vaginal discharges, and also in the bladder and intestine, more especially in infantile and other forms of diarrhœa. It has also been found in gangrene of the lung and in hydropneumothorax. Its pathological bearing is probably unimportant.

LAMBLIA INTESTINALIS, also a pyriform organism (10 μ to 16 μ, by 5 μ or even 12 μ), having one side of the larger end scooped out into a kind of sucker, is provided with four pairs of flagella; one pair springs from the anterior pole, two pairs from the posterior margin of the sucker, and one pair from the pointed posterior extremity. The flagella all trend backwards. The parasite can swim with ease; its usual condition, however, is one of rest, attached by its sucker to the summit of some intestinal villus, usually in the duodenum or jejunum, less frequently in the ileum. It occurs in man; also in the cat, dog, sheep, rabbit, and

FIG. 52. — *Trichomonas vaginalis.* —After Köllıker.

in several of the other smaller rodents. It multiplies by longitudinal division, passing from one host to another as an oval encysted body (10 μ to 15 μ, by 8 μ to 9 μ) (Fig. 53), in which condition it is found in the large intestines and fæces. It is doubtful if lamblia, though frequently present in the intestinal canal in great profusion, has any pathological importance.
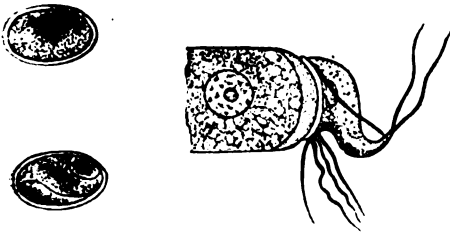
FIG. 53.—*Lamblia intestinalis.*

BALANTIDIUM COLI.—This infusorian is of an oval form, measuring from 70 μ to 200 μ in length, by 30 μ to 90 μ in breadth. It is composed of a finely granular protoplasm enclosing a reniform nucleus, two contractile vacuoles, particles of fatty matter, and alimentary débris. The ectoplasm is covered with short cilia subserving locomotion, and the direction of food towards the funnel-shaped indentation or mouth situated at the broader end. It multiplies by conjugation and fission. This parasite is not uncommon in the cæcum and colon of pigs, and has occasionally been found in man; generally it has been met with in association with diarrhœic or dysenteric conditions, pro-

FIG. 54.—*Balantidium coli*, with widely opened peristome (dorsal view).—Leuckart.

bably because such stools are those which are most frequently subjected to microscopical examination. There is no sufficient reason, so far as known, for assigning to it a serious pathological rôle. It has been treated with more or less success by enemata of quinine, or of salicylic acid (1 to 1000), and also by naphthaline by the mouth.

ANNULOIDA.

CESTODA.

Zoology.—The cestodes or tape-worms are long, ribbon-like animals, which in their mature form, with rare exceptions, inhabit the intestinal canal of vertebrates.

Each tape-worm (Fig. 55) consists of a minute, bulbous head (*scolex*), and a long, flat, and many-jointed body (*strobila*).   For purposes of fixation,
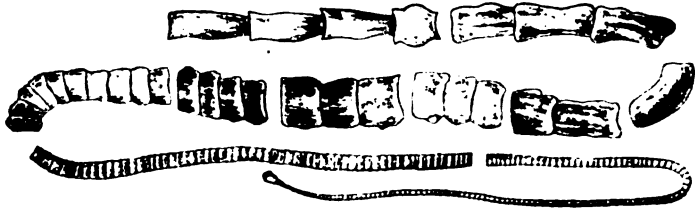
FIG. 55.—Tape-worm form of *Tænia saginata s. mediocanellata.*—Leuckart.

the fore part of the head is provided with two or four suckers, and generally, though not always, one or more circlets of hooklets surrounding in some species a central proboscis (Fig. 56).   The strobila or body is composed of joints (*proglottides*), which are developed serially and continuously from the posterior part of the head.   Each joint contains male and female
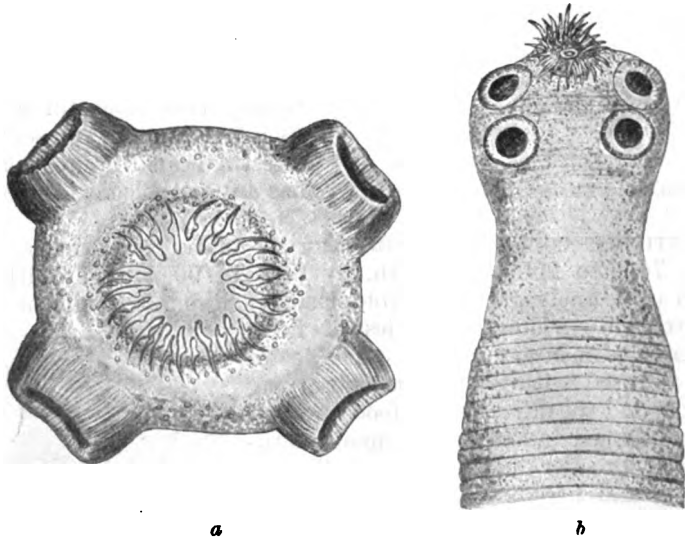
a   *b*
FIG. 56.—(*a*) Apex and hooks of *T. solium ;* (*b*) head of *T. solium.*
(× 35.)—Leuckart.

sexual organs (hermaphrodite); to this extent, although articulated to the joints before and behind, it is a complete and independent animal in itself.   The young proglottides or joints—that is, those nearest the head—are immature, and generally very minute; in some instances almost thread-like.   As the joints become older, and therefore further

down the strobila, they become progressively broader, longer, thicker, and sexually more mature. Thus a tape-worm is broad at one end, the posterior, that is where the segments are mature, and almost filiform at the other—the head or immature end. There is no mouth and no alimentary canal, nourishment being derived by absorption from the alimentary juices in the intestine of the host. The rudimentary nervous and excretory systems are continuous throughout the entire length of the parasite.

As the terminal joints mature they break away singly or in strings, escaping spontaneously, or being expelled in the dung of the host. The ova contained in the now free proglottides escape in various ways, and, if fortune favour, finally enter a suitable intermediate host. The medium in which the ovum gets access to its special intermediate host differs in different species. In some species the ova are poured out on the ground; in others they find their way into water; in others, again, they are conveyed in food. In some they enter the stomach of the intermediate host whilst still in the proglottis. By the action of the digestive juices of the intermediate host the shell of the ovum is dissolved off, and the minute,
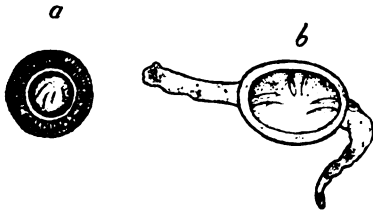
FIG. 57.—Embryo containing egg (*a*) of *T. solium* (without yolk skin); (*b*) of *T. nymphœa*. (× 400.)—Leuckart.
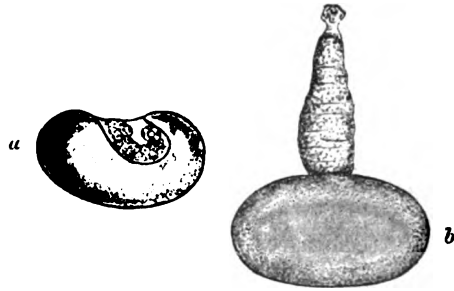
FIG. 58.—(*a*) The common bladder worm of the pig with invaginated head (× ½); (*b*) the same, with evaginated head (× 2).—Leuckart.

six-hooked embryo which each ovum contains is liberated (Fig. 57). The embryo thus freed works its way into the vessels and tissues of the intermediate host, and finally comes to rest in some appropriate tissue or organ. Herein it undergoes a somewhat complicated metamorphosis, in the course of which the six hooklets are got rid of, and the embryo in most instances acquires a cystic structure (*Cysticercus, Hydatid*). Finally, at that pole of the embryo which is opposite to that previously occupied by the six hooklets, one or, as in the hydatid-forming tape-worms, many scolices or heads, exactly like the head of the parent tape-worm, are developed (Fig. 58). In this condition the parasite may remain encysted for a considerable time. If now the intermediate host be eaten by an appropriate vertebrate, the scolex or scolices are set free, and, attaching themselves by the suckers and hooklets, with which they are provided, to the mucous surface of the intestine of the definitive host, rapidly grow into tape-worms. In one family of tape-worms, *Bothriocephalus*, there is no cystic formation in the intermediate host, the larva lying free in the tissues.

About a dozen species of tape-worms have been found in man. Only three of these, *Tœnia mediocanellata*, *Tœnia solium*, and *Bothriocephalus*,

are proper to him, or, from their frequency, possess much clinical importance.

T. MEDIOCANELLATA (*T. saginata*) is sometimes designated the beef tape-worm, from the circumstances that its immature or cystic stage is passed in the muscles of the ox. When mature, this parasite measures from 4 to 10 metres in length. It is made up of some 1200 to 1500 proglottides or joints, the terminal or more mature of which have a length of from 15 to 20 mm., and a breadth of from 6 to 8 mm. The
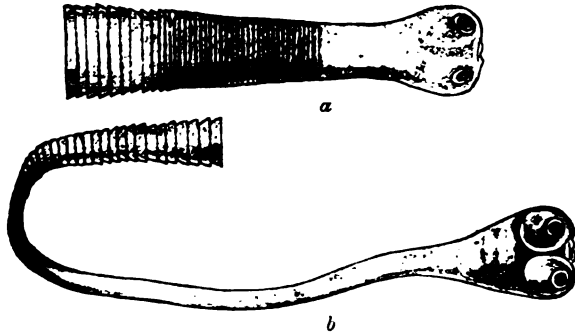
FIG. 59.—Head of *Tænia saginata* in contracted (*a*) and extended condition (*b*). (× 8.)—Leuckart.

proglottides at the centre of the strobila are the broadest. Traced upwards, they gradually fine down to a very narrow and delicate ribbon, which terminates in a pear-shaped head, provided with four suckers (Fig. 59). There are no hooklets on the head; hence the name, *T. inermis*, occasionally given to this tape-worm. The genital pores open on the margin of the proglottides, and can usually be readily seen.

T. mediocanellata is conveyed to man in raw or imperfectly cooked, measly beef (Fig. 59), that is, beef containing the "measle" or cysticercus.

FIG. 60.—*Cysticercus tæniæ saginatæ*, embedded in the muscle. (Nat. size.) —Leuckart.

After the cystic portion of the cysticercus is dissolved off in the stomach of the human host, the head attaches itself to the mucous membrane. The worm now grows so rapidly that in two months it attains maturity. It then begins to give off daily, and for an indefinite number of years, some eight to twelve ripe proglottides, each of them crowded with ova (38 by 30 μ) having a thick striated shell, and containing a minute six-hooked embryo. The proglottides, on escaping (usually singly) from the bowel, spontaneously or in the fæces, creep about on the ground or in the clothes, forcing out their ova, often through a rent, as they contract. The ova thus get scattered about on the grass or elsewhere, and so obtain, perhaps, an opportunity of attaining their appropriate intermediate host, the ox, in the connective tissue of whose muscles and viscera they assume their cysticercus form.

T. mediocanellata is found wherever oxen are kept, more especially where the cattle are badly tended, where beef is eaten raw or imperfectly cooked, and where the habits of the people expose their cattle to the infection.

T. SOLIUM, or the pork tape-worm, measures usually about 3 metres, sometimes 6 or 8 metres, in length. The proglottides number about 850 in an ordinary specimen; those about the middle of the worm attaining a breadth of 8 mm., the narrower but more elongated terminal joints being from 10 to 12 mm. in length by 5 mm. in breadth. The head (Fig. 56), which is furnished with four suckers, is readily distinguished from that of *T. mediocanellata* by the double row of twenty-six to twenty-eight hooklets which surround the somewhat prominent rostellum. The genital pores open marginally. As in *T. mediocanellata*, the uterus consists of a longi-

tudinal trunk with lateral branches; but whereas in *T. mediocanellata* these branches are straight, and do not subdivide, in *T. solium* they ramify dendritically. The ovum of *T. solium* is almost round, measuring 30 μ to 35 μ; the thick striated shell encloses a six-hooked embryo.
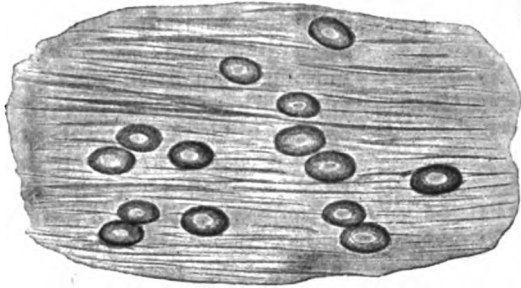
FIG. 61.—Measly pork. (Nat. size.)—Leuckart.

The cystic phase of this tape-worm is usually found in the pig; but it occurs also in many other mammals, including man. It is known as *Cysticercus cellulosæ*, and occurs in the connective tissue of the muscles and viscera and elsewhere (Fig. 61). It forms an ellipsoidal vesicle, 6 to 10 mm. in length, varying in size a good deal, according to the amount of pressure it is subjected to. In man, besides in the muscles, it is met with in the eye, which it may destroy; in the brain, as a peculiar ramifying cyst (*C. racemosus*), causing in many instances a variety of nervous symptoms; and in many of the other viscera, including the heart. When it lies under the
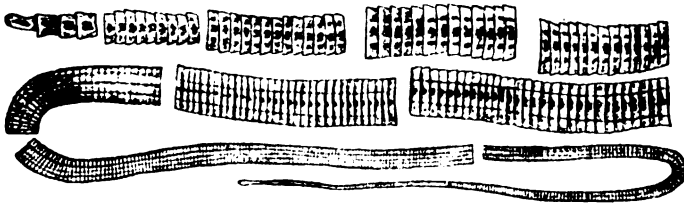
FIG. 62.—*Bothriocephalus latus.*—Leuckart.

skin it forms little pea-shaped swellings, whose nature is often unsuspected till they are excised and carefully examined.

T. solium is usually contracted from eating raw or underdone pork. The dirty habits of the pig afford a ready explanation of its special proneness to *C. cellulosæ* infection.

BOTHRIOCEPHALUS LATUS, or the fish tape-worm, attains a great length, 6 to 10 metres, sometimes even 16 metres (Fig. 62). It is also remarkable for its great breadth (10 to 12 mm.), and for the relative shortness of the proglottides (4 to 5 mm.), which in a full-grown specimen number from 3000 to 4000. The terminal segments are narrower and longer than those

higher up the strobila, and are furnished with two well marked, laterally placed, suctorial grooves. The head of the worm is flattened and club-shaped. The uterus when distended with ova is thrown into a series of radially arranged folds, forming what is known as the uterine rosette, towards the forepart of which, on the flat surface of the worm, are placed in close apposition the male and female openings. The ova, 68 μ by 45 μ, are brown, thick-shelled, ellipsoid, and operculated. The six-hooked embryo is not developed until the ovum has been in water for some weeks or months, according to temperature. When ripe, it forces back the operculum, and becomes a free, swimming animalcule, moving about by means of the innumerable and very long cilia with which it is covered. On being swallowed by certain kinds of freshwater fish—pike, burbot, perch, trout, etc.—it penetrates their muscles, and develops into a ribbon-shaped larva, 8 to 30 mm. in length. This is virtually the head and neck of the future bothriocephalus. It lies unencysted between the muscular fibres of the intermediate host. Unlike the other tape-worms, the larval bothriocephalus has no cysticercus form. On being swallowed by man, or by some animal, as the dog or cat, it grows into a mature tape-worm.

FIG. 63.—Club-shaped head of *B. latus.* (*a*) Seen from the flat edge; (*b*) from the surface. (× 8.) —Leuckart.

The geographical distribution of *B. latus* is somewhat restricted, being influenced, doubtless, by the ichthyophagus habits of the inhabitants of special districts. It is found principally on the shores of the Baltic, around the Swiss lakes, in North Italy, Bavaria, Poland, Turkestan, Japan, and recently on the banks of Lake Ngami, South Africa. In some of these places a very large proportion of the inhabitants are affected.

FIG. 64.—Ovum of *B. latus,* with yolk cells and shell. (× 300.) — Leuckart.

T. NANA.—The foregoing tape-worms are normally parasitic in and proper to man. Besides these, however, certain tape-worms, whose normal habitat is in some of the lower animals more or less intimately associated with man, occasionally find their way into the human alimentary canal, and there develop and attain maturity. The best known of these is *T. nana* (Fig. 66), which is believed to be identical with *T. murina* of the rat, and which has frequently been found in man, especially in children, in certain warm countries, including Egypt, Servia, Italy, Sicily, the United States, Brazil, Siam, etc. It is a very minute cestode, 12 to 20 mm. in length by 0·5 mm. in breadth, and with about 150 joints.

The head is spherical, and carries a rounded retractile and prominent rostellum, surrounded by a single row of twenty-two to twenty-eight minute hooklets.

FIG. 65.—Larvæ of *B. latus* from the pike. (*a*) and (*b*) with extended, (*c*) with contracted head. (*a*) nat. size, (*b*) and (*c*) × 3.— Leuckart.

T. FLAVOPUNCTATA is another, but rarer, visitor to man. It is also supposed to be normal to the rat, in which it is known as *T. leptocephala*. It measures from 20 to 40 cms. in length, the ripe proglottides being about 3·5 mm. in breadth and proportionately very short, but

becoming longer and narrower posteriorly. The proglottides towards the forepart of the strobila are characterised by a yellow spot, the distended receptaculum seminis. The ova, 0·06 mm., are smooth, have a double outline, and enclose a six-hooked embryo. The head is without hooks, and carries four suckers.

T. MADAGASCARIENSIS is another tape-worm which of late years has been found in man some eight times, and in countries very far apart—in Mayotte, Mauritius, Siam, and British Guiana. The larval form is
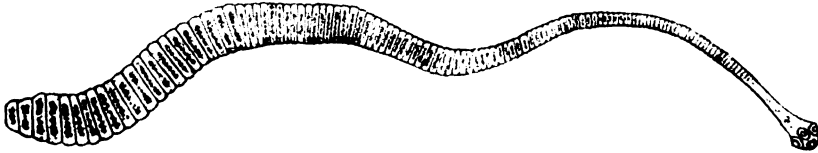
FIG. 66.—*Tænia nana.*—Leuckart.

believed by Blanchard to occur in some insect; he suggests the cockroach. The mature worm is from 25 to 30 cms. long, having some six hundred joints, which are considerably broader than they are long. The head carries a rostellum surrounded by a double circle of hooklets. The four suckers are round and large. The sexual opening is marginal. The normal host of this tape-worm is unknown; it is supposed to be a bird.

B. MANSONI.—This is the larval form of a bothriocephalus whose mature form is proper probably to some carnivorous animal. It is a long ribbon-shaped organism, 364 mm. by 12 mm. The writer found many specimens of this parasite in the subperitoneal connective tissue of a Chinese; Baelz also extracted one from the urethra of a Japanese. A similar, or an identical, parasite has lately been met with by Daniels in a Guiana Indian.

Besides these, other cestodes have occasionally been found in man; they are so rare, however, that they cannot be said to have any pathological importance or to be more than curiosities.

Symptoms.—Apart from the appearance of proglottides in the stools, in many instances the presence of a tape-worm gives rise to no symptoms whatever. On the other hand, these parasites at times seem to be associated with abdominal discomfort, dyspepsia, colicky pains, diarrhœa alternating with constipation, capricious appetite, foul breath, and so forth. In yet other cases a variety of nervous symptoms, including epileptiform seizures and even mental aberration, may result apparently from the presence of a tape-worm. In a proportion of instances, particularly in bothriocephalus infection, there is developed a peculiar form of hæmolytic anæmia, in some cases of a profound character, bothriocephalus anæmia.

Diagnosis.—The diagnosis of the particular species of tape-worm present in any given case may be arrived at by a careful examination of the proglottides. *B. latus* is at once recognised by the breadth of the proglottides and by the position of the sexual openings on the surface of the proglottis. In both *T. solium* and *T. mediocanellata* the sexual opening is

marginal; but in the former the lateral branches of the uterus are arranged dendritically, whereas in *T. mediocanellata* they are straight.

Treatment.—For a few days before instituting specific anthelmintic treatment, it is advisable to endeavour to get rid of any mucus that may be covering the parasite to be attacked. A light diet, and a few doses of sulphate of soda, will generally suffice for this. On the night before the anthelmintic is administered, the patient should go to bed fasting, or with only a cup of milk for the evening meal. The drug selected is best given in the early morning, and on an empty stomach. Male fern is the anthelmintic principally relied on; if properly administered, it is usually successful. It is best given in emulsion, or in milk, in doses of half a drachm at a time, and repeated every half-hour for four times, the last dose being followed by a smart cathartic. Kousso, if the drug is quite fresh, is also a good anthelmintic. The dose is from 4 to 6 oz. of the official infusion. Pomegranate decoction (2 oz. of bark to the pint of water), 6 oz. three times in succession at intervals of half an hour, is often effective. Its alkaloid, pelletierine, in from 5 to 7 grs., is said to be very reliable; it is somewhat intoxicating, and therefore not quite safe for children. The dose of turpentine, formerly much in vogue in the treatment of tape-worm, though now rarely used, is from 2 to 4 drms. in capsules or emulsion. For young children the safest, and a very effective, anthelmintic is bruised pumpkin seeds; the dose is an ounce made up as an electuary.

It is well for the patient to remain lying down until the intoxicating effects of these drugs, in some instances very pronounced, have passed away, and until the bowels have been freely moved by a cathartic. After the operation of the latter, search should be made in the stools for the head of the worm; unless this is found, no matter though yards of proglottides have been passed, there can be no assurance that this, the most important part of the parasite, has been got rid of, or that proglottides will not reappear in the stools some six weeks later.

TREMATODA.

Zoology.—These, with one exception (*Bilharzia hæmatobia*), are flat, fluke-shaped, hermaphrodite parasites (Fig. 67). They possess two suckers,

FIG. 67.—*Distomum hepaticum.* (Magnified.)

an anterior or oral placed at one extremity of the oval body, and a posterior or ventral placed on the ventral surface behind the former, and generally in the neighbourhood of the sexual opening. The alimentary canal opens at the anterior or oral sucker. The simple mouth leads to a short

œsophagus which divides, the two branches coursing along the lateral borders, one on each side, and terminating cæcally near the posterior end of the parasite. An excretory system of vessels unites into a single trunk which opens posteriorly. The greater part of the worm is occupied by the male and female organs.

Those distomes which inhabit man are all of them oviparous. The *eggs*, carried out of the body of their human host in the excreta or in morbid discharges, find their way into water, where in due course a *ciliated embryo* escapes, and swims about seeking out its appropriate intermediate host. The latter is usually some fresh water mollusc or arthropod. This the embryo contrives to enter, and therein, after getting rid of its ciliated covering, becomes converted into a *sporocyst* (Fig. 68), or into a somewhat similar structure called a *redia*. The redia differs from a sporocyst in being provided with a rudimentary mouth and alimentary canal. In due course certain germ cells in these sporocysts or, it may be, rediæ, evolve into what are known as *cercariæ*—minute tailed organisms with rudimentary suckers like those of the future fluke. In time the cercariæ escape from the intermediate host, and either enter a second animal, or attach themselves to some vegetable, and become encysted. If the cercariæ are now swallowed by the appropriate definitive host, they develop into mature distomes.
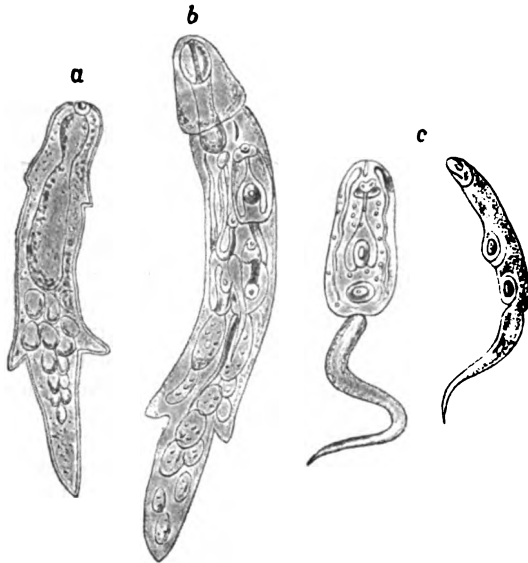
Fig. 68.—Rediæ. (*a*) with germs ; (*b*) with *cercariæ* in the interior ; (*c*) free *cercariæ*.—Leuckart.

DISTOMUM HEPATICUM.—Though proper to the sheep, *D. hepaticum* is sometimes found in other animals, and also, though rarely, in man. Its normal habitat is the bile ducts ; these it dilates and thickens, giving rise at the same time to enlargement of the liver, vomiting, diarrhœa, ascites, jaundice, emaciation, and fever, and in many instances leading to death. The parasite is known as the "liver fluke," and the disease in sheep as "rot."

D. hepaticum is long, brown, leathery, flat, leaf-shaped, broader anteriorly than posteriorly, and covered with minute spines directed backwards. It measures from 15 to 30 mm. in length by 4 to 13 mm. in breadth. The ventral sucker lies close behind the oral, which is placed at the free extremity of a sort of beak-like protuberance. The large, brown, operculated eggs (0.13 mm. by 0.08 mm.) escape in the bile and fæces. On being hatched out, the embryo enters the body of a certain fresh water gastropod mollusc (*Limnæa truncatula* and allied species), in which, from sporocyst and rediæ, the cercariæ are ultimately developed. The latter escaping, or perhaps while still in the mollusc, are passively transferred in

grass or water to the stomach of the sheep, or it may be to that of man. Thence they find their way into the bile ducts, where they ultimately develop into the mature parasite, setting up the morbid changes referred to. Should they happen to be present in sufficient numbers in the human subject, doubtless they would give rise to a dangerous disease similar to " rot " in sheep.
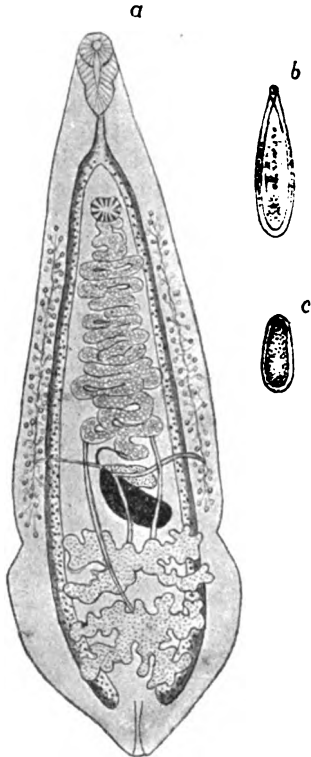
D. LANCEOLATUM has been found some five times in the bile ducts of man. Owing to its smaller size, it is not so formidable a parasite as the preceding. It measures 8 to 10 mm. in length by 2 to 2·4 mm. in breadth, the broadest part being posteriorly. It is further distinguished from *D. hepaticum* by its thinness, suppleness, and absence of cuticular spines. The ova (0·04 by 0·03 mm.) are dark, double outlined, operculated, and contain a ciliated embryo, the intermediate host of which is supposed to be *Planorbis marginatus.*

D. CONJUNCTUM, apparently a parasite of the Indian pariah dog, has been reported as occurring in the dilated bile ducts of man. It measures 9·5 mm. by 2·5 mm., and is covered with minute spines. The ova (0·034 by 0·021 mm.) are double outlined and operculated.

D. SINENSE is not very uncommon in natives of Japan and China, and has also been found in East Indians. In some instances of high degrees of infection it has proved a formidable parasite, giving rise to dilatation of the bile ducts, enlargement of the liver, and a cachexia corresponding to that of sheep rot, and characterised by fever, diarrhœa, anæmia, and dropsy, terminating after a time in death. The parasite measures 18 by 4 mm., and is readily distinguished from *D. conjunctum* by the complete absence of cuticular spines. The ova (0·03 by 0·016 mm.) are granular, double outlined, and operculated.

FIG. 69.—*Distomum sinense.*

FIG. 70.—*D. buski.* (Nat. size.)

D. CRASSUM is the largest of the distomes occurring in man. It measures 4 to 7 cms. in length by 1·7 to 2 cms. in breadth. It has been found in China, Borneo, the Malay Peninsula, India, and British Guiana. It is oblong in shape, fleshy, brown, and devoid of cuticular spines; it may be further identified by the close approximation of the oral and ventral suckers. The ova (0·125 by 0·075 mm.) possess granular contents enclosed in a very delicate operculated shell. The habitat of this parasite is the alimentary canal; possibly it is responsible for the dyspeptic symptoms and diarrhœa with which it has been found associated.

D. HETEROPHYES, an exceedingly minute (1·15 by 0·7 mm.) distome with a proportionately very large ventral sucker, occurs in man in Egypt. The ova (0·026 by 0·01 mm.) are reddish brown, and communicate their colour to the parasite. *D. heterophyes* lives in the small intestine. Apparently it gives rise to no morbid symptoms.

D. RINGERI (*D. pulmonale, D. westermanni*) (Fig. 71), a very thick, fleshy distome, 8 to 10 mm. by 5 to 6 mm., having a double outlined operculated ovum (0·08 by 0·1 mm.), inhabits the lungs of man and certain carnivora in Japan, Corea, China, and the Island of Formosa. It lives in tunnels connected with the bronchi. Into these bronchi the ova are poured, escaping thence in the sputum. After passing some weeks in fresh water, a ciliated embryo is developed, which at maturity, by forcing back the operculum of the shell, escapes and swims about in the water. Nothing further of its life-history is known.

Symptoms.—*D. ringeri* gives rise to what at times is a formidable kind of hæmoptysis. Patients in whose lungs this parasite occurs are
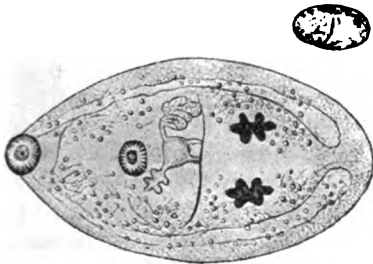
FIG. 71.—*D. ringeri.*—Leuckart.

FIG. 72.—Ova of *D. ringeri* in sputum.

affected with a chronic cough and peculiar brown, viscid, pneumonic-like expectoration, in which the microscope discovers myriads of the characteristic ova (Fig. 72). · In addition to the cough and expectoration, which are a permanent feature, the patient is liable to occasional attacks of sudden hæmoptysis. This may be so profuse as to lead to pronounced anæmia, and even to endanger life. Furthermore, high degrees of infection may end in extensive fibrotic changes in the lungs, and may, by predisposing to other forms of lung disease, indirectly prove fatal. This parasite has also been found in the cortex of the brain, where, from the irritation and pressure produced by the exudation it creates around it, it may give rise to a variety of cerebral symptoms, including Jacksonian epilepsy, which sooner or later terminate in death. *D. ringeri* has also been found in the testes, and in the peritoneum.

AMPHISTOMUM HOMINIS has been found in India inhabiting the cæcum, appendix, and ascending colon, to the mucous membrane of which it attaches itself by the relatively enormous ventral sucker. It is a minute parasite, measuring 5 to 8 mm. by 3 to 4 mm. The ventral sucker referred to is placed at the extreme posterior end, and is the most

prominent and characteristic feature about the worm. The ova measure 0·15 by 0·07 mm., and are operculated. Apparently this parasite is of no pathological importance.

BILHARZIA HÆMATOBIA (*D. hæmatobium*). This important parasite is confined to Africa and its island dependencies, including Mauritius, to Arabia, and to a limited district in Persia. It is particularly prevalent in Egypt, and has often been found in Europeans who have visited that country. It occurs in certain districts in Tunis, in·the Sahara, in South Africa, and on the West Coast. It gives rise to the disease known as "bilharzia disease," or "endemic hæmaturia."

Unlike the other distomes affecting man, *Bilharzia hæmatobia* is bisexual, the female—a long (20 mm.) filiform animal—being partially enclosed in a gynæcophoric canal produced by the infolding of the lateral borders of the shorter (15 by 1 mm.), stouter, and cylindroid male worm. The normal habitat of *Bilharzia* is the portal veins and its branches, where, by careful search, it may be found in considerable numbers (up to 300, Kartulis).

The ova (Fig. 74, *a*), which are minute (0·16 by 0·06 mm.), brown

FIG. 73.—*D. hæmatobium*, male and female, the latter in the canalis gynæcophorus of the former.—Leuckart.
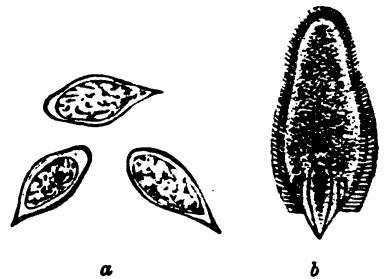
FIG. 74.—(*a*) Ovum, and (*b*) free embryo of *Bilharzia.*

bodies, provided with a very characteristic terminal spine, but without operculum, contain a ciliated embryo. They escape into the outer world in the urine and also in the fæces of the host. When urine containing these ova is mixed with water, the embryo (Fig. 74, *b*) escapes from the egg through a longitudinal rupture in the shell, and swims about. Nothing definite is known as to its intermediate host, nor as to its future life history.

The exact process by which the ova of *Bilharzia* contrive to get out of the human body has not been satisfactorily explained. Apparently the gravid female seeks out the venous radicles in the rectum and bladder, and there deposits her eggs, which subsequently work their way, possibly aided by the spine with which they are provided, into bladder and bowel.

In consequence of the presence of vast numbers of ova, and the attendant irritation to which they give rise, the walls of the bladder become thickened and the mucous membrane inflamed, roughened, and, occasionally, the seat of phosphatic deposit, the entire organ undergoing all the morbid alterations incident to chronic cystitis. The ureters, vesiculæ seminalis, uterus, and even the pelvis of the kidney may be affected. Sometimes the ova form the nucleus of urinary calculi. In

the rectum, a chronic proctitis may be established by the presence of the parasite or of its ova, and minute polypoid growths arise in consequence.

Symptoms.—As a general rule, *Bilharzia*, beyond giving rise to a slight degree of urinary irritation and hæmaturia, is not a very troublesome parasite. Occasionally, however, in consequence of the chronic cystitis it induces, bilharzia infection is attended with much suffering, and, by causing secondary changes in the kidneys, or stone in the bladder, may even endanger life. In some of the endemic districts, particularly Egypt, owing to the frequency of the infection, the aggregate amount of suffering and the severe disease it induces, bilharzia infection becomes a serious matter.

From implication of the rectum, a sort of false dysentery is frequently present; but in the vast majority of cases the leading symptoms are to be referred to the bladder. In slight degrees of the infection the patient is conscious of a feeling of urinary irritation, most pronounced at the end of micturition, the passage of the last few drops of blood-tinged urine being attended with a sense of heat. In more severe infections, especially during exacerbations of the attendant cystitis, the suffering is very great, resembling that in stone. The desire to micturate is almost incessant, and the urine (ammoniacal, perhaps) is loaded with muco-pus, sometimes containing much blood. Ultimately a continuance of suffering may wear out the patient, or secondary kidney affection may prove fatal.

On holding the urine of a bilharzia patient up to the light, it is seen to contain numerous little white shreds or strings of mucus. These under the microscope are found to be studded with the characteristic brown, spined ova. If such urine be allowed to stand, on sampling the sediment, ova can be readily detected. In mild infections, the best plan of finding the ova is to catch in a watch-glass the last few drops of urine while the patient strains; this almost invariably contains an abundant supply. Bilharzia once contracted is rarely got rid of. The cystitis it gives rise to and the presence of ova in the urine, may persist for twenty or even thirty years.

Diagnosis.—The presence of the various trematodes above described, although it may be suspected, cannot be affirmed with certainty unless the parasites themselves or their ova are found in fæces, urine, or sputum, as the case may be. In patients from the East, enlargement of the liver, failing other and more obvious explanation, should suggest the possibility of *Distomum sinense* infection; chronic cough, rusty sputa, and occasional hæmoptysis, pulmonary distomiasis. In patients from Africa or Mauritius, chronic cystitis and hæmaturia should suggest a microscopic examination of the urine for bilharzia ova. The discovery of the ova of trematodes in the stools is, of course, diagnostic of the presence in the liver or alimentary canal of their special parental forms.

Prophylaxis.—The boiling of drinking-water and the avoidance of uncooked food, including vegetables, are obvious precautions indicated by our knowledge of the life history of these parasites.

Treatment.—Intestinal flukes, *Distomum crassum* and *Amphistomum hominis*, are amenable to thymol, which, in their case, may be administered, as in ankylostomiasis (p. 549). Flukes occurring in the bile ducts cannot be dislodged by treatment.

Pulmonary distomiasis is also incurable. Severe muscular efforts, as they tend to cause hæmoptysis, are contra-indicated. Symptoms of cerebral tumour occurring in the subject of pulmonary distomiasis should suggest the presence of a distomum tumour in the brain, and the feasibility of excision.

Bilharzia disease is equally incurable, although much can be done by judicious living to avert cystitis and severe hæmorrhage. The patient should be a total abstainer; he should avoid a rich dietary and give up all forms of exercise entailing succussion or necessitating pressure on the perineum, as riding. He should drink freely of bland diluents, particularly during intercurrent attacks of cystitis, and keep to his bed at such times. Should there be much muco-pus in the urine, the daily washing out of the bladder with warm boric acid solution is indicated, salol being administered internally at the same time. Severe and persistent chronic cystitis may be much relieved by cystotomy.

NEMATODA.

Zoology.—These are long, slender, bisexual organisms. The cylindrical body tapers towards both extremities, at one of which is placed the mouth, at or near the other the anus. They consist of a musculo-cutaneous tube, in the interior of which lie (*a*) the straight alimentary canal; (*b*) in the case of the male, the single convoluted testis opening into a cloaca, common to it and the alimentary canal at the anus; (*c*) in the case of the female, two much convoluted ovarian tubes, stuffed with ova and embryos at various stages of development, and opening into a short vagina which usually terminates in a vulva near the anterior end of the worm. Excretion is carried on by two vessels, one on either side, lying in a vacant space—the lateral lines—in the muscular wall; anteriorly these vessels unite and open at a point, the vascular pore, a short distance behind the mouth. The male worm, which invariably is the smaller, has a sharply curved or spiral tail, provided with one or two protrusible chitinous spicules lodged in the cloaca, which serve to fix the female *in coitu.* In addition, the tail of the male is also generally furnished with two rows of papillæ, placed on either side of the anus. Sometimes there are membranous appendages of a more or less complicated nature at the head or tail.

Certain of the nematodes are oviparous; others are viviparous, or ovo-viviparous. The embryos are minute and eel-like in shape and movement. In many instances, prior to entering the definitive host they pass through an elaborate metamorphosis in the body of another animal, the intermediate host; in other instances, the embryo matures outside the body, and gives rise to a non-parasitic generation, whose offspring, on being swallowed, revert once more to the parasitic condition. In others, the ova, gaining access in food or water to the alimentary canal of the definitive host, are there hatched and develop into mature parasites.

ASCARIS LUMBRICOIDES, or round worm (Fig. 75), common in most, is very common in many countries, particularly in the tropics. It inhabits the upper part of the small intestine, occasionally wandering into the stomach or into the lower part of the bowel. Both sexes are plump, cylindrical, grey or pinkish in colour, shining, transversely and finely

striated, and somewhat rigid. They taper gradually towards both ends, particularly towards the mouth, the three lips of which are provided each with a papilla.

The female form, much the larger, measures from 16 to 45 cms. in length by 6 mm. in diameter. The male, readily recognised by his inferior dimensions and sharply curved tail, measures from 15 to 25 cms. in length by 4 mm. in diameter; two short spicules protrude usually from the cloaca, on either side of which is a row of some seventy minute papillæ. In both sexes, the interior vessels can readily be seen shining through the musculo-cutaneous body wall.

FIG. 75.—*Ascaris lumbricoides*, female.—Leuckart.

The ova (Fig. 76) (0·075 mm. by 0·058 mm.) vary a good deal in contour, some being barrel-shaped, others oval or round. They possess a very thick, rough, multiple outlined brown shell and granular contents. If placed in water in a warm place and exposed to the light, in the course of one to six months, according to temperature, an embryo is developed. Desiccation does not kill the embryo, which escapes only on being transferred to the stomach of man, where it develops in the course of a month into a sexually mature parasite. The ova are present in the fæces in prodigious numbers, and can readily be recognised by the microscope ($\frac{1}{2}$ in. objective).

Symptoms.—These parasites are most prone to occur in children; adults, however, are by no means exempt. In warm countries few escape occasional invasion of this sort. In some instances there may be only one or two; in other instances they occur in dozens, or even in hundreds. Occasionally they crawl into the stomach, and at times, passing up the œsophagus, escape by the mouth or nostrils. They are sometimes vomited, especially in severe fever; sometimes they escape spontaneously in the fæces. Although generally so, *A. lumbricoides* is not always a harmless parasite. Cases are on record in which they

FIG. 76.—Egg from *A. lumbricoides* fresh from the fæces.—Leuckart.

produced suffocation by creeping into the rima glottidis; they have been known also to enter the bile ducts, producing jaundice and even hepatic abscess. Sometimes they have penetrated the gut and set up peritonitis. Such events, however, are rare accidents. As a rule, the ascaris causes little disturbance; at most, vague abdominal discomfort. In children they may give rise to peevishness, foul breath, capricious or perverted appetite, irregularity of the bowels, feverishness, irritation of the nose and anus, and occasionally convulsions.

Treatment.—A few doses of santonin—$\frac{1}{2}$ to 5 grs., according to age—is a certain cure. It is well to give a purge a few hours after the santonin.

A. MYSTAX, normally parasitic in the carnivora (cat, dog, etc.), sometimes

occurs in man. It is very much smaller (male, 4 to 6 cms. by 1 mm.; female, 6 to 12 cms. by 1·7) than *A. lumbricoides*, from which it is further distinguished by peculiarities in the tail, as well as by a very conspicuous cutaneous wing on each side of the head. The ova (0·068 by 0·078 mm.) are covered with a sort of network resembling in pattern the mace on a nutmeg.

OXYURIS VERMICULARIS, or thread-worm (Fig. 77), like *A. lumbricoides*, is a cosmopolitan parasite, occurring most frequently in children. Entering the alimentary canal as an ovum, it is hatched out in the stomach; passing thence into the intestine, it rapidly attains maturity. After copulation the male worm usually dies; the female, however, moves on to the cæcum, where she remains until ovulation is complete. She then descends to the rectum, where, in some instances, her ova (Fig. 78) are deposited in, and escape with, the fæces.

In other instances the parasite spontaneously emerges from the anus and wanders about over the skin in the neighbourhood, giving rise to much irritation. In consequence of the scratching so provoked, the worms are ruptured, and the ova, clinging to the fingers, are, during the picking of the nose and mouth, so frequent a concomitant of thread-worms, unconsciously transferred to the patient's mouth. The parasitism is thus kept up by auto-infection. It may also spread by contiguity to other individuals, as, for example, among children of the same family or school; or it may be introduced through contamination of the food or water supply. Unless special precautions are taken against repeated auto-infection, a constant succession of thread-worms may persist in the same individual for years, and even into adult life. It only takes fifteen days, dating from the introduction of the ova into the stomach, for the parasite to mature and begin to appear in the stools.

FIG. 77.—*Oxyuris vermicularis.* (a) Male (nat. size); (b) male (magnified); (c) female (nat. size); (d) female (magnified).—Leuckart.

The female worm measures from 9 mm. to 12 mm. in length, by 0·4 mm. in breadth; the male from 3 mm. to 5 mm. in length, by 0·16 mm. to 0·2 mm. in breadth. In both sexes, under the microscope, the head is seen to be furnished with a characteristic cuticular appendage, shaped like the mouthpiece of a Turkish tobacco-pipe. In the female the anus is placed at the base of the sharp-pointed straight tail. In the
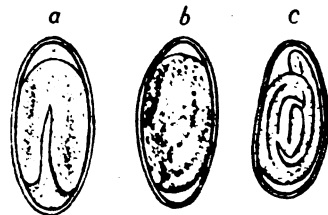
FIG. 78.—Eggs of *O. vermicularis.* (a, b) freshly laid; (c) with developed embryo.—Leuckart.

male the anus is terminal, and the tail, which is provided with a single spicule and six pairs of papillæ, is truncated and generally coiled up.

The anal irritation set up by these worms is often exceedingly troublesome, and from the broken sleep and constant worry it entails, may seriously impair the health. It is always most troublesome when the child is warm in bed, the warmth of surface seemingly inducing the worms to wander out by the anus. If the stools of such a patient be inspected, numerous slowly moving parasites, looking like short lengths of white thread, can be detected; these are the female oxyurides. The male are not only few in number, but, owing to their small size, are easily overlooked.

The ovum (Fig. 78) (0·05 mm. by 0·016 mm. to 0·024 mm.) generally contains a differentiated embryo. It is further distinguished by its treble outlined shell; this is distinctly flattened on one side, being defective as regards the middle layer on the other or more convex side.

Treatment.—An important step in treatment is the recognition of the way by which an infection is kept up. The attendants of children should be thoroughly informed on this point, and instructed to make provision, either by means of drawers or by tying up the end of the night-dress, against the child reinfecting itself. An infected child should not be allowed to sleep with other children. The nocturnal anal irritation is best prevented by smearing some weak form of mercurial ointment, or carbolic oil, or similar drug about the anus; these kill the emerging worms. Those parasites still in the cæcum cannot very well be dislodged; but those that have descended to the rectum are easily got rid of by enemata administered every night, or, later, every third night, of salt water, infusion of quassia, of water containing a few drops of tinct. ferri perchloridi, lime water, vinegar and water, etc. Occasional aperients should be given at the same time.

EUSTRONGYLUS GIGAS (or giant strongyle) has been found six or seven times in man. It is especially a parasite of the ichthyophagous carnivora, in whom it occurs in many countries. Its habitat is the kidney, which it destroys, converting the organ into a bag of pus, and giving rise to renal pain, purulent urine, and hæmaturia. The foveolated ova (0·065 mm. by 0·043 mm.) appear in the urine, and are diagnostic of the condition. These formidable nematodes attain enormous dimensions; the male, recognised by the terminal copulatory bursa and solitary spicule, measures from 14 to 25 cms. in length, by 4 to 5 mm. in diameter; the female, 25 cms. to 1 metre in length, by 4·5 to 12 mm. in diameter. This parasite, if its presence has been recognised, could be easily removed by surgical means.

ANKYLOSTEMUM DUODENALE (*Dochmius duodenalis,* or the tunnel-worm). (Fig. 79). On account of the grave cachexia to which it frequently gives rise, and on account of its frequency, this is one of the most important animal parasites affecting man. It is extremely prevalent in many warm countries; in Europe, though very much rarer, it has been the cause of many epidemics of the characteristic and often fatal anæmia with which it is associated. It has been found as far north as the 51st parallel; probably it has a corresponding southern limit. In Egypt it is almost general. In many parts of India it is present in 75 per cent. of the adult

population.   In Africa, in the West Indies, in Brazil, and in many other tropical countries, it is probably equally prevalent.

The ankylostomum inhabits the upper part of the jejunum, and, to some extent, the duodenum and ileum, to the mucous membrane of which it attaches itself by a powerful and remarkable buccal armature.   It derives its nourishment from the blood it freely ingests.   From time to time it shifts its hold, the abandoned bite oozing a little blood, and thereby leading to further depletion of the patient.

FIG. 79. — *Ankylostomum duodenale,* male and female.—Blanchard.

The male worm (Fig. 80) measures from 6 to 11 mm. in length, by 0·4 to 0·5 mm. in diameter; the female, which is three times as numerous as the male, measures 7 to 15 mm. by 1 mm.   Both sexes are white or reddish brown in colour, and cylindrical in shape, the posterior end being the broader.   The tapering neck ends in a cup-shaped expansion, or mouth capsule, the lips of which are provided with four hooks and two teeth.   The caudal end of the female terminates in a short spine, at the base of which is the anus; the vagina opens considerably in advance of

FIG. 80.—Male *ankylostomum duodenale.*

this.   The caudal end of the male is expanded into a trilobed, umbrella-like bursa; at the bottom of this is the cloaca, from which two very long and delicate spicules emerge.   The female emits a vast number of ova (Fig. 81) (0·06 by 0·04 mm.), which appear in the fæces, and can be recognised readily by their regular oval form, delicate, single outlined, transparent shell enclosing two to eight greyish yolk spheres.   Very active rhabditiform embryos are developed soon after the ova-charged fæces escape from the host.   After two moultings the embryo passes into a larval condition, and if now transferred in dirty water, or in earth, or by dirt-soiled hands or food to the human stomach, rapidly develops into the mature parasite.   Some authorities assert that the

FIG. 81.—*A. duodenale.* —Sonsino.

ankylostomum can, for one or two generations, reproduce itself heterogenetically whilst outside the human body.   It is difficult to determine how long the individual parasites live in the host; certainly it is for many months, possibly for several years.

If these parasites are present in the intestine in large numbers, or if

the subject of the infection is poorly nourished, or of feeble constitution, the persistent drain of blood and the dyspeptic conditions entailed by the injuries to the mucous membrane and possibly the absorption of some poisonous substance eliminated by the worm, gradually or more rapidly lead to the production of a cachexia which persists and increases so long as the stock of parasites is kept up. Ultimately the infection may prove fatal from pure anæmia, or, it may be, by predisposing to other disease. In many, without causing actual disease, it nevertheless leads to a condition of debility unfitting for active labour. Ankylostomiasis is now the recognised cause of much of the anæmia which is so common in the natives of tropical countries, and as being at the root of such affections as *Egyptian chlorosis*, the *cachexia aqueuse* of the West Indian negroes, and of other similar conditions.

Symptoms.—The subjects of extensive ankylostomiasis frequently suffer from forms of dyspepsia in which epigastric tenderness, borborygmus, capricious, inordinate, or perverted appetite are apt to be prominent symptoms. Many exhibit a craving for earth, or lime, or similar sub-stances—*pica, geophagy.* Gradually all the symptoms of a profound anæmia are evolved, including languor, pallor, breathlessness, vertigo, tinnitus, syncope. Though the surfaces are pale, the body is plump and, towards the latter stages, puffy from œdema. If the stools in such a case be examined, there is usually no difficulty in finding with the microscope numerous ova (Fig. 81) of the parasite. In all cases of tropical anæmia, for which the cause is not obvious, such an examination should be made. It sometimes happens in long-standing cases of ankylostomiasis, or of cases which, presumably, at the outset were cases of ankylostomiasis, that the parasites, the original cause of the anæmia, have died out. In such cases ova will, of course, not be found; it is to be presumed that the lesions in the alimentary canal, the fatty degeneration of the heart muscle, and other organic changes, the result of the prolonged anæmia, keep up the cachexia and prevent recovery.

Treatment.—The patient should be placed for a day or two on fluid diet, and a mild saline administered. Next morning, fasting, three or four doses of from 15 to 30 grs. each of thymol, in cachets or emulsion, are administered at intervals of one to two hours, the last dose, if the bowels have not acted freely, being accompanied by a purge. Many ankylostomes will be expelled, and can readily be recovered from the stools by washing. If, after ten days or a fortnight, ova are still present in the stools, the thymol course must be repeated. As a rule, this second course is not required, the patient, under judicious feeding, rapidly regaining strength and colour.

Certain precautions are to be observed in the administration of this valuable drug. Thymol often produces a form of intoxication ; therefore, while under its influence, the patient should be kept lying down. Though feebly soluble by the intestinal juices, thymol is readily dissolved by alcoholic fluids, by ether, turpentine, oils, glycerin, chloroform, and alkalies ; therefore these things must be carefully eschewed until the drug has been voided. Neglect of this obvious precaution has led to fatal poisoning. In cases in which the patient is very low, it is well to post-pone the use of the drug until, by careful feeding and by rest, strength has been somewhat restored.

Filix mas, formerly much used as a vermifuge in ankylostomiasis, is still occasionally employed in doses similar to those for tape-worm.

It is not so efficient as thymol, and, like that drug, has also the drawback of occasionally producing toxic symptoms. It has the additional disadvantage of costliness and liability to adulteration or to inertness.

Prevention.—From the fact that the ankylostomum enters the body in dirty water, on dirty fingers, dishes and food, in the endemic area great care should be exercised to keep the water supply uncontaminated by fæcal matter. Suspicious water should be boiled. Coolies and others must not be allowed to eat with earth-soiled hands, or out of dirty dishes. Proper latrines should be provided, and all fæcal matter destroyed by fire or buried. Soil contaminated with fæces should be dug over, or otherwise dealt with so as to secure destruction of the ova or larval ankylostoma.

TRICHOCEPHALUS DISPAR, or whip-worm (Fig. 82), so called from its peculiar shape, inhabits the cæcum and, occasionally, other regions of the alimentary canal, to the surface of which it sometimes attaches itself by transfixing the mucous membrane with its long capillary neck; usually it is found lying loose on the surface of the mucosa.

The sexes resemble each other as regards length (35 to 45 mm.), but the male can be distinguished by his coiled up caudal end from the

FIG. 82.—*Trichocephalus dispar, in situ.*— Leuckart.

FIG. 83.—*T. dispar.*— Sonsino.

extremity of which a single spicule, enclosed in a trumpet-shaped sheath, can be seen, with the microscope, to be protruding. In the female the tail tapers gradually to a sharp point, the anus being subterminal; the vagina opens at the root of the long hair-like neck. In both sexes the posterior part of the worm is much the thicker, and contains the sexual organs.

The ova (Fig. 83) (0·05 by 0·025 mm.) are oval, smooth, thick-shelled, dark brown, and without differentiated embryo. They are readily recognised by their somewhat pointed ends, which exhibit a clear, plug-like protuberance filling up a gap in the shell. The ova mature in water, but only after a very long time—twelve to eighteen months. When the embryo has completed development, on transference to the human stomach the shell of the egg is dissolved off and development proceeds. In the course of from four to five weeks the parasite becomes sexually mature, her ova escaping in the fæces, in which they can readily be recognised with a low power of the microscope.

T. dispar is cosmopolitan. In many European countries it is present in half the population. In tropical countries it is almost universal. The prevalence of the parasite depends in great measure on the character of the water supply.

T. dispar, apparently, gives rise to no symptoms, and is of no patho-

logical importance—a fortunate circumstance, seeing that it is but slightly amenable to anthelmintics.

TRICHINA SPIRALIS.—This nematode, which in natural condition seems to be more especially a parasite of the rat, is acquired by man through eating raw or imperfectly cooked pork, pork sausages, lard, or other preparation of swine's flesh. The dangerous disease it gives rise to is called *trichiniasis* or *trichinosis*.

If the muscles of a pig affected with trichina be closely scrutinised with a lens, they are seen to be besprinkled with numerous white specks. If a portion of muscle, after teasing out in normal salt solution and compression under a cover-glass, be placed under the microscope, these white specks are found to be minute (0·4 by 0·25 mm.) lemon-shaped cysts (Fig. 84 *b*), lying lengthways between the fibres, each containing a coiled-up cylindrical worm, occasionally two or more worms, which, on the slide being slightly warmed, exhibit slow movement. The worms measure about 1 mm. in length. An alimentary canal runs from the narrower oral end to the thicker abruptly truncated anal end; rudimentary organs of generation can also be distinguished.

If a portion of the affected flesh be given to a dog, or other mammal, the cysts are digested off by the gastric juices. The worms survive and pass into the duodenum. In the course of one or two days they attain sexual maturity, measuring at this time about 1·5 mm., the female (*c*) being somewhat the larger. The male is provided with two caudal appendages, by which the female is secured during coitus. This function effected, he dies. The female, however, continues to grow, ultimately attaining a length of from 3 to 4 mm. On the sixth or seventh day after ingestion the first young are born. They are minute, lancet-shaped organisms (1 by 0·006 mm.), rounded anteriorly, and tapering towards the tail (*a*). The

FIG. 84.—*Trichina spiralis.* (*a*) Embryo; (*b*) intermediate form; (*c*) sexual form. (Unimpregnated female.)—Leuckart.

female during some six weeks emits a continuous stream of young, which penetrate the walls of the alimentary canal, and, crossing the peritoneal cavity, travel along the connective tissue spaces. Finally, arriving at the muscles, they encyst themselves, forming a capsule out of the hyperplasia of connective tissue cells provoked by the irritation of their presence. Encystment is complete in about eighteen days from the date of infection. By this time the young trichina has increased in size, and so far advanced in development, that, on being transferred to the stomach of a suitable mammal, it is capable of proceeding to

sexual maturity. The encysted trichina retains its capacity for development for many years—five to twenty, it is said; ultimately, however, it dies, and the capsule becomes cretified.

The pillars of the diaphragm, and the intercostal muscles, especially the diaphragm, are the muscles most affected. But the parasites are to be found in every muscle of the body (with the exception of the heart, which is rarely invaded), and more especially towards their tendinous ends. They are not confined, however, to the muscles, but encyst themselves in the panniculus adiposus also, and even in the walls of the alimentary canal; lard and sausage skins, therefore, may prove infective and dangerous.

The encysted trichinæ possess great powers of resistance. Decomposition, chemical substances such as pickling fluid, freezing, and temperatures up to 80° C. fail to kill them. Unless a ham or joint of pork. be thoroughly cooked, any trichinæ that may be in the centre of the piece will not be killed. A safe rule as regards prevention of trichiniasis is to cook such viands thirty-five minutes for every kilogramme of weight.

Wherever rats and pigs are found,—that is, practically everywhere, —trichiniasis may occur. Owing to the thorough cooking to which preparations of pork are subjected in Britain, the disease is rare in this country; but in Germany, where pork sausages and ham are frequently consumed in a half-cooked or raw state, until stringent inspection of the carcases of all swine killed for the market was instituted, trichiniasis was not uncommon.

Symptoms.—Minor degrees of trichiniasis are probably often overlooked; but the clinical features of the severer degrees of infection, especially if the disease occur as a circumscribed and sudden epidemic, are so distinctive, that it should be readily recognised. The severity of the individual cases varies very much according to circumstances. The larger the amount of infected food consumed, and the greater the number of larval trichinæ the meat contains, the more severe will be the disease. On the whole, trichiniasis is less dangerous to children than to adults. The cases range in severity from a mild gastro-intestinal derangement, followed by rheumatic-like muscular pains, to a choleraic-like disease followed by intense general myositis, a typhoid condition, and death. In a case of moderate severity, it is possible to recognise three stages: first, one of gastro-intestinal irritation; second, one of myositis; and third, one of convalescence.

Within a few hours of swallowing trichiniased flesh, symptoms of acute irritation of the upper part of the alimentary canal set in. There is purging and vomiting, foul tongue, anorexia, colic, and prostration. These symptoms correspond with the growth and sexual activity of the parent trichinæ, and the subsequent penetration of the intestinal canal by their migrating offspring. Such symptoms may continue for a week or ten days, or even longer. Then follow symptoms indicative of the invasion of the muscles by the parasites. There is pain, tenderness, and hard swelling of the muscles, together with fever, the thermometer rising to 103° or even to 106° F. Movement becomes intensely painful; and, owing to implication of the diaphragm and intercostal muscles, respiration may be seriously interfered with. Similarly mastication, deglutition, phonation, and ocular movement may all become impaired or impossible from the same cause. The patient lies in bed with limbs

semiflexed and motionless. About the eighth day there is marked puffiness of the face, especially about the eyelids; occasionally there is chemosis in the latter situation. This puffiness subsides in a few days; but towards the fourth or fifth week, general œdema, sometimes very pronounced and resembling that of acute nephritis, sets in. This œdema may come and go. At the same time there is profuse sweating, and sudamina and various skin eruptions, as pimples and boils, may appear. Wasting and a typhoid condition are now pronounced, and may be accompanied by delirium or stupor. In adults insomnia is apt to be a marked feature, doubtless in great measure caused by the pain in the muscles. Children, however, are always somnolent. Bronchitis or pneumonia may also supervene.

If the patient survive, improvement may be looked for about the sixth week; that is, when the trichinæ have completed encystment, and the myositis begins to subside. In mild cases improvement may set in earlier; on the other hand, it may be delayed for two or three months. Death may occur in the early stages from the violence of the initial choleraic symptoms. Usually it does not occur till the height of the myositis, when it may be brought about by asphyxia from implication of the respiratory muscles, or by some intercurrent complication such as pneumonia. A tedious marasmus may prove fatal at a later period.
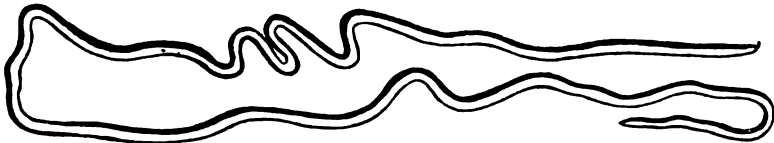
Fɪɢ. 85.—Guinea-worm. (Reduced.)—Leuckart.

The mortality in trichiniasis varies in different epidemics, and within wide limits—from 1 or 2 to 30 per cent.

Diagnosis.—The diseases with which trichiniasis is most apt to be confounded are cholera, acute rheumatism, typhoid fever, and beriberi. Whenever there is a doubt, the stools should be searched for adult trichinæ; or, if necessary, a small piece of muscle excised and examined with the microscope. Recent observations in America have established the striking fact, that the acute stage of trichiniasis is accompanied by a remarkable increase of eosinophile leucocytes in the blood, a circumstance which has been successfully applied in diagnosis.

Treatment.—If the case is seen early, with the view of getting rid of any trichinous food that may still remain in the stomach, quickly acting emetics are indicated. Free purging, so long as it is to be presumed that there are parent trichinæ in the alimentary canal, should be encouraged, best by large doses of calomel. Thymol, given as in ankylostomiasis, would probably be of great service at this stage. The subsequent stage of myositis, and the concomitant typhoid condition, are to be treated on general principles.

FILARIA MEDINENSIS (Fig. 85) (*Dracunculus medinensis,* or guinea-worm), unknown as an indigenous parasite in Europe, is common in many parts of Africa, especially on the West Coast, in India, Persia, Turkestan, and Arabia. It is found in one or two places in Brazil, but nowhere else in

America. It special habitat is the connective tissue of man, and occasionally of some of the larger mammalia.

The guinea-worm attains a length of from 1 to 6 ft., and a diameter of $\frac{1}{16}$ in. It is white, smooth, polished, extensile, cylindrical, abruptly truncated at the head, and terminates in a short, stout hook at the tail. A slender alimentary tube runs along the entire length of the worm, from the punctiform mouth to close to the tail, where it merges into the body wall; there is no anus. The greater part of the cylinder formed by the musculo-cutaneous body wall is occupied by the relatively huge uterus, which, extending from head to tail, is packed with myriads of coiled up embryos (Fig. 86). In the mature worm, whatever may be the case in early life, there is no vagina. The male parasite is unknown.

When the young guinea-worm enters the human body, presumably in
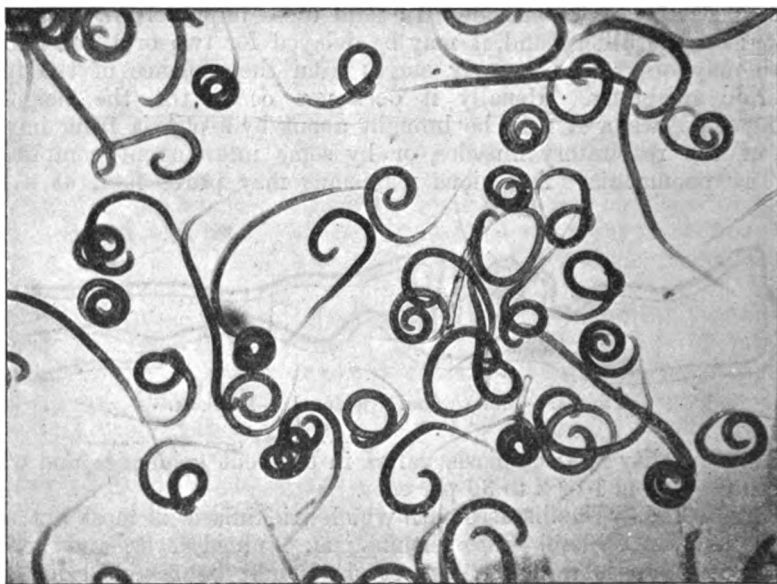
FIG. 86.—Embryos of guinea-worm.

drinking water, she is probably of microscopic dimensions. Analogy indicates the conclusion that, after penetrating the walls of the stomach or intestine, the young worm works its way into the connective tissue, to remain there in a more or less passive condition until the uterine contents have attained a certain stage of development. When or where impregnation is effected is not known. In the course of about one year the now matured and gravid worm proceeds to migrate to the position most favourable for affording her young access to the medium—fresh water—in which the first stage of their lives is passed. Occasionally, though rarely, she may appear about the scrotum, abdomen, arms, or even the scalp; in 95 per cent. of cases she descends to the legs or feet. She then drills a small hole in the derma, the epidermis becoming raised up as a bleb over the site of the hole. When, after a day or two, this bleb ruptures, a superficial ulceration or excoriation — half an inch to an inch in diameter —is disclosed; in the centre of this sore the hole referred to can be

detected. In some instances, on the rupture of the bulla, the head of the worm is seen protruding from the central hole; usually, however, this is not so, the head being retracted and out of sight. If now the foot of the patient be placed in cold water, or if a little cold water be allowed to trickle on to the skin in the vicinity of the sore, in the course of a few seconds a droplet of whitish fluid is seen to well out from the central hole; in other instances, a slender tube is slowly protruded, and, under the influence of a *vis a tergo*, becoming tense, presently ruptures, a similar whitish fluid escaping. This tube is undoubtedly the uterus, prolapsed through the mouth in consequence of the contraction of the musculo-cutaneous structures of the worm, in response to the stimulus of the cold water. If a little of the whitish fluid is placed under the microscope, it will be found to contain enormous numbers of coiled-up passive embryos, which, on the instillation of a little water under the cover-glass, immediately commence to swim about with great activity (Fig. 86). These embryos measure $\frac{1}{30}$ of an in. in length, by $\frac{1}{1000}$ of an in. in breadth. Anteriorly, they are rounded off; posteriorly, they taper to a long, slender swimming tail, at the root of which two peculiar gland-like organs are apparent. An alimentary canal is distinctly visible, but no organs of generation can be made out. The cuticle of the embryo is somewhat coarsely, transversely striated. The body is not cylindrical, but compressed laterally, so that, as the animal swims with its longer transverse diameter in a vertical position, the embryo looks much narrower when in motion than when at rest and lying on its flat surface. These embryos will live for several weeks, especially if placed in muddy water.

If a number of embryos are placed in water in a watch-glass along with a fresh-water cyclops, they attack the cyclops, and, penetrating the joints of the latter, enter its body cavity and ultimately undergo a remarkable metamorphosis. They cast their skins two or three times, get rid of their swimming tails, acquire a more complete alimentary canal, rudimentary organs of generation, and a peculiar tripod-like caudal appendage. It is presumed that, after this metamorphosis is completed, the young guinea-worm is ready for transference to the human stomach.

When the parent guinea-worm, after penetrating the skin, in the course of a fortnight or thereby has emptied her uterus, she exhibits a tendency to quit the body of her human host. At this stage she can be withdrawn with comparative ease; prior to this she resists attempts at extraction, and frequently ruptures under the strain of misdirected efforts made for her removal. As a rule, only one guinea-worm presents at a time, but cases of multiple infection are common; two or three are by no means unusual, and sometimes dozens may be present.

Just before the guinea-worm appears, the patient may be attacked with fever and urticaria. If properly managed, the presence of this parasite may cause but little trouble; but if, in consequence of injudicious attempts at extraction, the worm should be ruptured, and occasionally even without such interference, violent inflammation of the limb ensues, leading to abscess, sloughing of the tissues, and, as a consequence of this, not infrequently, contractions and deformities. Death may result from septic trouble.

Treatment.—It is evident that in guinea-worm districts the drinking water must be carefully attended to, and boiled or filtered if from a suspicious source. The subjects of guinea-worm must not be allowed to bathe their sores in the vicinity of the water supply.

Formerly it was the practice to attempt to wind out the worm by attaching the protruding head, so soon as it could be laid hold of, to a piece of wood, and making a few turns of this daily. This practice is dangerous, and should not be attempted until the uterus of the parasite has emptied itself; then, but not before, the natural tendency of the worm to come out may be encouraged by the winding-out method. Recently Emily has introduced what he and others maintain is a much more expeditious and safer way of dealing with guinea-worm. If the worm is presenting, he injects her, by means of a hypodermic syringe introduced into her mouth or body, with perchloride of mercury solution, 1 in 1000. This kills the worm, and renders her track aseptic; in a few hours, if so treated, she can easily be removed by judicious winding-out. If she has not penetrated the skin, although her coils can be detected in the subcutaneous tissue, the perchloride solution is injected at several points as near the body of the worm as possible. This also kills her. She may then, after a few hours, be cut down on and removed by careful traction, or she may be left alone; in the latter event the dead body is absorbed like a piece of aseptic catgut.

Occasionally the guinea-worm dies before she has pierced the skin. Abscess may ensue; or the parasite may be absorbed; or it may become cretified, and for years remain as a hard innocuous convoluted cord, easily felt beneath the skin.

FIG. 87.—*Filaria loa.* (Nat. size.) — Argyll Robertson.

FILARIA LOA (Fig. 87).—In many parts of the West Coast of Africa, the natives, and occasionally the European residents, are the host of this parasite. It resides in the connective tissue, and apparently has the habit of wandering all over the body. Sometimes a little local swelling and irritation indicate the presence of the worm in a finger; at another time a similar local swelling and irritation show that it has travelled to the forearm or elsewhere. A favourite resort of the parasite is the subcutaneous fascia about the orbit, and not infrequently the subconjunctival connective tissue. When traversing the latter, the worm is plainly visible as it wriggles across the ball of the eye.

The female loa (30 to 40 mm.) is considerably larger than the male (25 by 0·3 mm.). In both sexes the integument is studded with numerous minute hemispherical bosses. The tail of the male is incurvated, and carries two short unequal spicules and five pairs of caudal papillæ. The uterus of the female contains a crowd of sheathed, sharp-tailed embryos closely resembling *F. nocturna* and *diurna.* In what way the embryos escape from the human body has not yet been ascertained. Although they have been sought for in the blood at all hours of the day and night, and in apparently suitable cases, hitherto they have not been found in the circulation. The life-history of this parasite is quite unknown.

When a loa visits the eye, its presence may give rise to considerable irritation, so that its removal is desirable. This is easily effected by cocainising the eye, at the same time seizing the conjunctiva and subjacent worm with fixation forceps. The conjunctiva is then snipped or incised, and the worm withdrawn. In the event of a loa presenting under the skin elsewhere, doubtless a hypodermic injection of bichloride of mercury solution (1 in 1000), made in the same way as for guinea-worm, would prove an efficient parasiticide.

RHABDONEMA INTESTINALE is an intestinal nematode, found in many warm countries, especially in diarrhœic conditions, and in association with *A. duodenale.* It is very minute, 2 by 0·04 mm. Its young, formerly known as *Anguillula stercoralis* (Fig. 88), are hatched out in the intestine of the host, and appear in the fæces as actively wriggling, sharp-tailed embryos. *R. intestinale* appears to be innocuous.

FIG. 88.—Embryo *Rhabdonema intestinale* in fæces. — After Golgi and Monti.

FILARLÆ SANGUINIS HOMINIS.—The young of at least four species of filariæ occur, as a normal feature in their life histories, in the human blood. They have been named *F. nocturna, F. diurna, F. perstans,* and *F. demarquaii.* Besides these, another form, closely resembling *F. demarquaii,* has been found under circumstances which make it possible that it belongs to an additional and independent species. On this assumption I have named this blood worm, provisionally, *F. ozzardi.* An adult filaria (*F. magalhæsi*) has also been found in the blood; so far it is impossible to be certain that this is not the adult form of *F. demarquaii.*

The hæmatozoal filaria embryos, though closely resembling each other, are nevertheless distinguishable by peculiarities in their morphological and physiological details. They are all of them long, sinuous, snake-like, extremely active organisms, ranging in size, according to species, from $\frac{1}{125}$ in. to $\frac{1}{75}$ in. in length, by $\frac{1}{5500}$ in. to $\frac{1}{3000}$ in. in breadth. In shape they are cylindrical, tapering posteriorly, and being somewhat abruptly rounded off anteriorly. Their transparent bodies consist of a delicately transversely striated, musculo-cutaneous structure enclosing a column of minute cells, in the continuity of which various interruptions can be made out in stained specimens, and also, though less readily, in the living and unstained animal. One of these interruptions near the anterior end has been named the "V spot"; a second, about the middle of the worm, and apparently produced by a long cæcal vessel, the "central viscus"; and a third close to the tail, the "tail spot."

F. NOCTURNA (Fig. 89) (*F. sanguinis hominis* of Lewis), and the diseases it gives rise to, are found in the tropics and sub-tropics. In some places it is rare, whilst in others it is present in from 10 to 50 per cent. of the population, its occurrence depending on the hydraulic conditions, the habits of the people, and the distribution of certain species of mosquito. It measures $\frac{1}{75}$ in. by $\frac{1}{3000}$ in. to $\frac{1}{3500}$ in., and is enclosed in a very delicate, transparent, structureless sheath, which, being considerably longer than the little animal it contains, dangles from head or tail, according to the degree of contraction or extension, and to the position for the time being of the body of the worm. The head end exhibits a peculiar movement produced by the retraction and protraction of a six-lipped prepuce and of a minute spine.

It is the habit of this worm to frequent the peripheral circulation only during the night (hence its name). Beginning to appear in the superficial capillaries about five or six in the evening, it increases in numbers up to midnight, diminishes in numbers towards morning, and disappears for the day about 8 or 9 A.M. During the day, as has been ascertained

by post-mortem examination, it retires to the lungs and larger arteries, where at that time it may be found in prodigious numbers. This phenomenon of diurnal appearance and disappearance has been named "filarial periodicity."

Filarial periodicity is an adaptation of the habits of the filaria to those of particular species of mosquito which act as its intermediate host. The female mosquito in feeding sucks up the filaria with the blood. So soon as the parasite finds itself in the stomach of the mosquito, it quits its sheath, thereby uncovering the cephalic armature alluded to; by means of this armature it is enabled to travel into the thoracic muscles of the insect. Arrived there, and lying passively between the muscular fibres, it undergoes a metamorphosis which eventuates in the elaboration of an alimentary canal, a four-lipped mouth, a three-lobed caudal end, great increase in size ($\frac{1}{10}$ in.), and eventually renewed activity. The filaria now quits the thoracic muscles, and, passing forwards, traverses the prothorax and neck of the insect, coiling itself up in the head just under the brain and at the base of the proboscis. Thence from the sixteenth to the twentieth day it passes into the proboscis, by means of which it is doubtless inserted into the tissues of a human host, when the mosquito next feeds on human blood. It is possible, though not likely, that a

Fig. 89.—*Filaria sanguinis hominis nocturna.* (× 160.)

few of the metamorphosed filariæ escape into water, and in this medium reach man. Arrived in man, the parasite passes, by penetrating the tissues, to its permanent habitat—the lymphatic trunks; here it grows into a sexually mature nematode (*F. bancrofti*) and in due course, after impregnation, emits its young—*F. nocturna.* The young, after passing along the lymphatics, appear in the blood.

F. BANCROFTI is a long, slender, filiform worm, in appearance like a white horse-hair. When newly removed from the body, it exhibits active wriggling movements. Its surface is smooth. The head is somewhat club-shaped, and is unarmed, having a punctiform mouth at its centre. The female worm is the larger, being 3 to 4 in. in length by about 0·185 mm. in breadth; the male is 2 to 3 in. in length by ·1 mm. in breadth. In both sexes the tail, after tapering somewhat, is abruptly rounded off, the anus being subterminal. In the female the vagina opens a short distance (1·2 mm.) behind the head. The tail of the male is provided with two unequal spicules; so far, no caudal papillæ have been made out.

Ordinarily these parasites give rise to no disease. Occasionally, however, particularly when present in large numbers, when unfortunately located, or when injured, they prove pathogenic. The young (*F. nocturna*), in many instances, are present in prodigious numbers; as many as 500 or 600 have been counted in a drop of blood. In such cases, large numbers of mature worms (*F. bancrofti*) have been found in the lymphatics. The young circulate freely, and do no harm to their human host; the mature parasite alone is pathogenic.

F. bancrofti gives rise to disease in three different ways. Sometimes, apparently in consequence of its death, it causes abscess—filarial abscess. Sometimes, by blocking the large lymphatic trunks, particularly the thoracic duct, it dams up the lymph stream; it thereby causes dilatation of the vessels in the implicated area, necessitating regurgitation of the contents of the thoracic duct through a compensatory anastomosis. Permanent varicosity—lymphatic varix—ensues. These varices sometimes rupture. If the varix happens to involve the urinary bladder, kidneys, or ureters, and rupture occurs, the contents of the varix escape into the urine, and chyluria is the result. If the varix involves the scrotum, lymph scrotum is produced. This is a sort of soft elephantoid thickening of the scrotum, the surface of which is studded with dilated lymphatics, which are prone to rupture spontaneously or as a result of injury. If the varix involves the groin glands, certain peculiar, soft, doughy swellings, apt to be mistaken for hernia, are formed—varicose groin glands. Lymphatic varices may form in other parts, as the legs, or surface of the abdomen; should the varices rupture, they lead to permanent or intermitting lymphorrhagia. Tumours similar to those in the groin may form in the axillæ. Occasionally somewhat similar but evanescent swellings, caused by temporary blocking of the lymphatics by the parent worms, may appear; such occur more especially on the arms. Chylous dropsy of the tunica vaginalis is an occasional result of rupture of a filarial varix in that situation. These various varices are apt to inflame, but they rarely suppurate. The symptomatic fever is very often acute, tends to recur at uncertain intervals, has a well-marked initial rigor, followed by severe, hot, and sweating stages; it is apt to be mistaken for malarial fever. With care a correct diagnosis, based on the concurrent lymphangitis, should be easily made.

There are strong reasons for believing that tropical *elephantiasis arabum* also is caused by *F. bancrofti;* but the *modus operandi* of the parasite in giving rise to the various forms of this condition is not so obvious. It seems probable that the lymphatic obstruction which eventuates in the elephantiasis, is caused by embolic plugging of the afferent lymphatics of the glands by ova prematurely emitted by a parasite that has been injured by a blow or otherwise. The ovum is of much greater diameter than the embryo filaria, and consequently cannot pass the glands. This embolism gives rise to lymph stasis, which, if the implicated part become inflamed through injury or septic infection, gradually leads to hypertrophy of the implicated integuments. The blocked lymphatics are incapable of removing the effused inflammatory products. Recurring attacks of lymphangitis and associated erysipelatoid inflammation may thus gradually build up an enormous swelling. In consequence of the lymphatic area containing the parasites being cut of by the embolic plugging of the glands, the embryos of the worm which had wrought the original mischief cannot enter from the blood; consequently,

elephantiasis arabum, although probably caused by the filaria, is not generally associated with the presence of *F. nocturna* in the circulation. On the other hand, the way to the blood being still open in chyluria, lymph scrotum, varicose groin glands, and other forms of filarial varix, in these diseases *F. nocturna* is generally to be found in the circulation. Occasionally, in cases of long standing, although the disease persists, the parasites die out.

In chyluria the patient passes a milky-looking, pinkish, or sanguino-lent, opaque urine, which usually sets into a blancmange-like jelly. The clot so formed gradually contracts, a scanty reddish deposit falling to the bottom, and a cream-like pellicle forming on the surface of the urine on standing. Oil globules, lymph corpuscles, and perhaps red cor-puscles like those of blood, are present in abundance, and very frequently filariæ are found in the deposit, or entangled in the fibrinous coagulum. The urine contains large quantities of albumin. This condition is liable to come and go at uncertain intervals, and to persist for hours, days, or months at a time. The appearance of chyle in the urine is generally preceded by aching in the loins and pelvis, and other sensations evidently symptomatic of distension by accumulated chyle and lymph in the enormous lymphatic varix which dissection has shown to be present in the abdomen and pelvis in this as well as in lymph scrotum, varicose groin glands, and other forms of filarial varix. Coagulation of chyle in the bladder sometimes causes retention of urine calling for catheterism. Chyluria is rarely directly fatal; but it is apt, if prolonged and excessive, to drain the patient and give rise to anæmia, debility, and great mental depression.

Treatment.—Many drugs have been vaunted as efficacious, but it is questionable if any medicinal substance can control lymphorrhagia from a gaping lymphatic in the urinary tract. Tincture of the perchloride of iron, tannic acid, gallic acid, salol, salicylate of soda, benzoic acid, ichthyol, chromic acid, methylene-blue, have all been recommended. To be of any service, it is evident that these drugs must be given in full doses. By far the most effectual, as well as rational, way of treating chyluria is to send the patient to bed and to insist on his keeping the recumbent position with the pelvis elevated; to place him on low diet, and to stop all fats and other chyle-forming foods; to restrict the amount of fluid; to purge gently with a saline; and to adopt such other measures as would be likely to lessen fluid pressure in the tense and leaking lymphatics.

The subjects of chyluria, and of the various other forms of filarial varix, should avoid all violent efforts such as are likely to lead to rupture of the engorged and thinned vessels. Pregnancy is prone to induce chyluria in filarial patients. Lymph scrotum and varicose groin glands should be excised if troublesome. It is well to bear in mind that their removal must increase the lymph pressure in the remainder of the lymphatic anastomoses, and therefore may eventuate in chyluria or in elephantiasis of a leg. These, as all forms of filarial disease, do best in cold climates.

In elephantiasis arabum there is a thickening of the skin and sub-cutaneous fascia, resulting, as explained, from imperfect absorption of inflammatory products in a lymphatic-blocked area. The disease is very common in countries in which *F. nocturna* is also common. It is per-manent, and tends to increase from recurrences, at longer or shorter intervals, of the inflammation, each attack adding a little to the bulk of the mass. The surface of the affected part becomes rough and glabrous.

The derma is dense, unyielding, and greatly hypertrophied; whilst the sub-cutaneous fascia is converted into a lax, blubbery-looking, dropsical tissue, traversed by irregular fibrous bands. The lymphatics are enlarged, the lymphatic glands hypertrophied and indurated. The arteries and veins may also be increased in size; and there may be various pressure changes in nerves, muscles, and bones. The parts most usually affected are the legs, one or both; the scrotum, which may attain enormous dimensions; the labia; more rarely the arms are attacked; and, still more rarely, the mammæ and isolated skin areas.

In the case of the legs and arms, elastic bandaging, elevation, and massage may help to keep the swelling under. When the scrotum, labia, or mammæ are seriously and inconveniently involved, they should be removed.

The prophylaxis of this as of all filaria disease lies in protection from mosquito bite and in the suppression of these insects.

F. DIURNA. — Morphologically indistinguishable from *F. nocturna*, this hæmatozoon is, nevertheless, an independent species. *F. diurna* appears in the peripheral circulation during the day only; a physiological feature exactly the opposite to the corresponding phenomenon in *F. nocturna*, and one pointing to a different intermediate host. It seems to be very common on the lower Niger and adjacent countries. The parental form is unknown; equally so the associated pathological conditions.
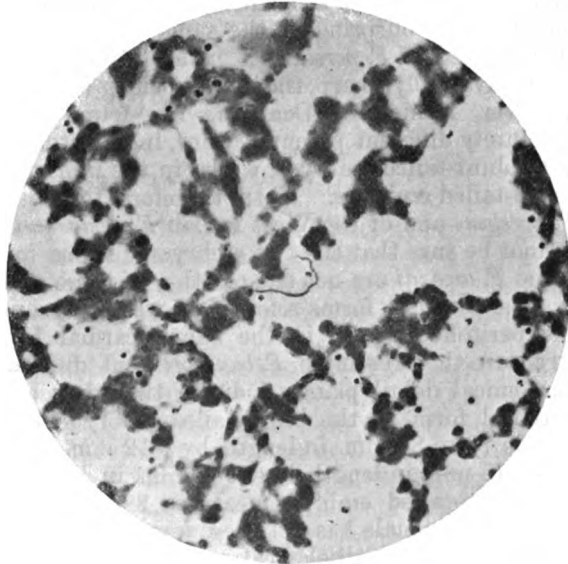
FIG. 90.—*Filaria sanguinis hominis perstans.* (× 160.)

F. PERSTANS.—Shorter and more slender (0·23 by 0·0045 mm.) than the preceding parasites, *F. perstans* further differs in not possessing a sheath, in having a truncated tail, in being endowed with locomotive habits as well as with remarkable powers of retraction and extension, and also in not exhibiting a diurnal periodicity.

F. perstans appears to be confined to certain extensive tracts in West Africa—particularly the Congo basin, where it is present in many places in quite 50 per cent. of the native population. I have also seen it in Europeans who had resided in that country. It occurs in Guiana (see *F. ozzardi*). The parental form resembles *F. bancrofti*. Very little is known of its pathological bearings. From the concurrence of their respective geographical ranges, and from other circumstances, it has been conjectured that *F. perstans* may in some way be responsible for that singular West African disease—sleeping sickness.

F. DEMARQUAII in size and habit resembles *F. perstans*. It differs, however, from the latter in anatomical characters, the tail being sharply pointed. In fact, *F. demarquaii* is like a diminutive *F. nocturna* without the sheath and diurnal periodicity. Hitherto it has been found only in the West Indies—St. Vincent and St. Lucia. Possibly it occurs in British Guiana, New Guinea, and West Africa. The parental form has not been identified with certainty. So far as known, *F. demarquaii* gives rise to no disease.

F. OZZARDI.—The blood in over 50 per cent. of the aboriginal Indians of British Guiana has been found to contain two minute filarial embryos— one morphologically identical with *F. perstans*, the other with *F. demarquaii*. From the circumstance that the two forms are almost invariably in association in the same host, it was at one time considered that they might be the offspring of the same parental form; in which case, seeing that the tail of *F. perstans* is invariably truncated, and that of *F. demarquaii* invariably sharp, they must belong to quite another species. Lately, however, Daniels of Demerara has found in these Guiana cases two absolutely different parental forms, in the uterus of one of which he found only blunt-tailed embryos, whilst in the uterus of the other he found only sharp-tailed embryos. Until, therefore, the parental forms of the African *F. perstans* and of the West Indian *F. demarquaii* have been identified, we cannot be sure that the two embryonic forms indicated by the provisional name *F. ozzardi* are not one or other of these parasites.

The parental forms referred to were found in the mesentery, beneath the peritoneum, and in the subpericardial fat. In general shape and structure they resemble *F. bancrofti*, but differences in measurement and anatomical detail plainly indicate that they are not this parasite. The parental form of the blunt-tailed embryo measures in the case of the female 70 to 80 mm. in length by 0·12 mm. in breadth; in the case of the male, 45 mm. in length by 0·064 mm. in breadth. The female parent of the sharp-tailed embryo measures 280 mm. in length by 0·45 mm. in breadth; the male has not been described.[1]

Hitherto no pathological condition has been recognised as depending on these parasites.

F. MEGALHÄSI.—The mature form of this parasite was found in Brazil in the left ventricle of a child, and was doubtless associated with hæmatozoal embryos; the latter were not described. The dimensions of the parasites were as follows:—Female, 155 by 0·66 mm.; male, 83 by 0·25 mm.

PATRICK MANSON.

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[1] Since the above was written, I have found the parental form of *F. perstans*. On comparing this with Daniel's parental form of the British Guiana blunt-tailed embryo, I find them to be identical.

SECTION III.

DISEASES CAUSED BY CHEMICAL SUBSTANCES.

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LEAD POISONING.

POISONING by metallic lead, apart from the inhalation of its fumes during the act of smelting, is rare except in the case of file-cutters. It is generally due to one or other of its salts. Lead poisoning is described under many names, *e.g.* plumbism, saturnine poisoning, colica pictonum, and colica pictorum.

History.—The use of lead has long been known. The recent finds of bars of lead in Derbyshire and Shropshire, stamped with the imperial arms of Rome, show that the early invaders of Britain were quite familiar with the metal. Mention is made in the writings of Galen and Vitruvius of drinking-water when conducted through lead pipes acquiring hurtful properties, and from this we infer that plumbism not only existed in the early part of the Christian era, but that one of its causes was distinctly recognised. One Roman architect, we are told, thus interdicted the use of lead, a proscription which to-day is as much called for as then, seeing how frequently plumbism has arisen among dwellers in towns from drinking water conveyed through lead pipes. In the five years ending 1890, there occurred 1822 deaths from accidental poisoning in England and Wales, and of these 541, or 29 per cent., were due to lead. During the five years ending 1895, plumbism caused 672 deaths in England and Wales.

Lead is a subtle poison. So numerous are the sources of the poison, and so gradually is the health undermined by it, that it is not until in some instances his constitution is profoundly affected by it that the individual is aware of what has taken place. The outbreaks of plumbism in some of our large towns, and the extent to which serious illness occurs among workers in white-lead factories, alike demonstrate the fact of the slow but sure operation of the poison. It is with lead as with most poisons—all into whose system it has gained entrance do not suffer equally. There is an individual and a family predisposition to plumbism, and to these might be added a sexual proclivity, for women, especially young women, seem to suffer more readily than men. A gouty diathesis pre-disposes to it, also poverty, alcoholic intemperance, and want of personal cleanliness on the part of lead workers.

Etiology.—It is unnecessary to enumerate at length all the sources of lead poisoning. Of these the principal are—(1) Contamination of the drinking-water at the gathering ground or in its transit, whereby, owing to certain physico-chemical changes having been induced in the water, its plumbo-solvency is increased, and (2) working among lead or its salts. The presence of a trace of iron or of nitrogenous compounds in water imparts a plumbo-solvent influence, which renders the water dangerous for human use if drawn through lead pipes.

The presence of lime salts in water prevents to some extent the interior of a lead pipe being injuriously acted upon by water, for an insoluble carbonate of lead is thus formed and deposited upon the metal. This, however, is readily dissolved by water containing the slightest trace of acidity, even carbonic acid itself. New lead pipes are more quickly influenced than those that have been in use for a time, and the same remark applies to a pipe made of lead from which all the silver has been abstracted; hence there is less danger in using pipes made from British lead than those from foreign ore. All these facts demonstrate how unwise it is for us to have our drinking-water conveyed through lead pipes or stored in lead cisterns, and the advisability of replacing this metal by some substitute such as iron or by glass-lined lead pipes. The presence of even very minute quantities of lead in drinking-water is dangerous, for experience has shown that plumbism is less due to the entrance into the system of one or two large doses of a lead salt, than to the continued entrance of very minute quantities over a lengthened period. Health may be lost by a person repeatedly drinking water that contains only $\frac{1}{100}$th to $\frac{1}{15}$th of a grain of lead per gallon. In one of my own cases severe symptoms followed the use of water which contained ·0028 gr. of lead per gallon. It is not necessary that the lead should be in solution. Some time ago I saw, in consultation, a lady who was suffering from a severe form of lead poisoning, due to a careless workman having left in the cistern several lumps of white-lead. In Queensland, epidemics of lead poisoning have been traced to the use of water that has been stored in galvanised iron tanks.

Of all our industries it is the white-lead factories that supply the largest number of cases, and the most serious types, of plumbism. In this country the manufacture of white-lead is carried on by what is known as the old Dutch process. The product thus obtained is renowned for its purity and whiteness. It is during the emptying of the " white beds," and more particularly the drying of the white-lead in what is called the " stoves," that the factory worker, inhaling the fine dust suspended in the atmosphere, is most prone to become affected. Six weeks spent in this occupation have to my knowledge proved fatal to young women.

The Potteries of Staffordshire have for long had an unenviable reputation for lead poisoning. Girls employed as "dippers' assistants" and " brushers off," also colourers and majolica paintresses, frequently become paralysed and blind. It is estimated that 300 to 400 cases of plumbism occur in the Potteries annually. Painters, too, are peculiarly prone to lead colic. Stühler of Berlin, who draws his statistics of plumbism from the reports of sick benefit societies, states that of 3000 painters in Berlin 313 were annually sick from this cause, equal to 10·4 per cent. Gautier found in Paris that out of 14,000 painters and varnishers, on an average 250 visited the hospitals on account of lead poisoning, and an equal number received treatment at home, giving a percentage of 3·5.

Printers' compositors have for long been known to suffer from plumbism, but whether this is due to absorption through the skin by handling the type, which contains lead, and becomes oxidised during wear, or is swallowed by eating with unwashed hands, has not been definitely settled. Fromm discusses the question, and alludes to Stumpf's analysis of the dust of printing-houses, which he found contained as much as 14·43 per cent. of lead. In a recent report to the German Board of Health, Faber states that he found in the dust collected from the floor 11·51 per cent., on a shelf in the room 6·59 per cent., and in the gangway between the desks in the composing-room of a newspaper office 4·7 per cent. of lead. Inhalation of the dust of the oxidised metal in all probability, therefore, plays the more important part in the causation of plumbism among compositors.

The use of canned foods, too, especially fruits, is a source of plumbism. As a result of the action of natural acids upon the tin or solder, lead is dissolved out and can be readily detected in the syrup. A child died after eating tinned sardines, and in the internal organs of the victim, as well as in the oil and sardines, Lowry of Baltimore found lead. Canned pears and apricots show the greatest amount of dissolved lead, pine-apples the least.

Lead gains entrance into the system through — the respiratory passages, by inhalation of the fumes during the smelting of the ore, or by breathing an atmosphere rendered dusty by the presence of lead salts; through the gastro-intestinal tract, by food and drink having been contaminated, or, in the case of the lead worker, by eating with unwashed hands; and through the skin when perspiring. Of these channels entrance by the respiratory passages is very important, also entrance by the stomach, the hydrochloric acid of the gastric juice converting any insoluble lead salts into the soluble chloride, which is readily absorbed. Lead is eliminated from the system by the kidneys and bowels; also by the skin, and occasionally by the milk.

Morbid anatomy and pathology. —Acute plumbism. —The morbid anatomy of acute plumbism is practically nil. After death from lead encephalopathy, beyond the brain being found shrunken, firm, and dry, or extremely pale and watery, as in uræmic poisoning, the cerebrum may present nothing unusual. On chemical analysis, lead may be detected in the brain; in some of my own cases it was absent. Lead is also found in the liver, kidneys, and bones; never in the blood serum, although, according to Binz, it is said to have been found in the red blood corpuscles. The heart and lungs present nothing abnormal; the small intestine at places is occasionally extremely contracted. The kidneys, on microscopical examination, present the appearances met with in early parenchymatous nephritis, namely, cloudy and fatty changes in the renal epithelia, accompanied in more chronic cases by evidence of interstitial and glomerular nephritis.

Chronic plumbism. —It is in the chronic plumbism that the kidneys are atrophied and the interstitial tissue excessive. The pathological changes at first are in the tubular epithelium and in or around the glomeruli. In this view I am supported by Charcot and Gombault, who in their experiments upon animals always found the tubular epithelium proliferating, and subsequently in the later stages the interstitial tissue increased. Coën and d'Ajutolo found the epithelia of the convoluted tubules swollen and disintegrating as early as the fifth day in animals poisoned by lead, and only in the later stages evidence of interstitial nephritis. Carl Hirsch has repeated these experiments, and he finds in the early stages of plumbism

the glomerular vessels extremely full, the epithelium of Bowman's capsule swollen, whilst outside the capsule there is an accumulation of small round cells. In all his cases there were swelling and disintegration of the tubular epithelium, hyaline and calcareous tube casts, along with cellular infiltration between the tubules. The opinion that in the early stages of lead poisoning, interstitial nephritis is the typical lesion of the kidney, is not the one that commends itself to me, nor to the authors just mentioned. The primary changes are undoubtedly epithelial. The liver is also the seat of pathological changes. In the early stages the hepatic cells are granular, and the seat of fatty degeneration, while later on there is evidence of an intercellular cirrhosis. On chemical analysis, lead is found most largely in the liver. During life the functional activity of the kidneys and liver is so impaired that animal poisons are retained in the system, to the influence of which upon the brain we must largely attribute the epileptiform seizures. In fatal cases of encephalopathy the brain may be dry on the surface, as already stated, and its convolutions appear as if compressed, or there may be some subarachnoid effusion, but where this is present the kidneys are usually at the same time affected.

Does the paralysis of lead poisoning depend upon a central or a peripheral lesion of the nervous system? Pathological opinion is divided upon this point. In old-standing cases of plumbic paralysis, the peripheral nerves have unquestionably shown marked increase of their connective tissue with atrophy of the nerve fibres. In the earlier stages, Charcot and Gombault described the peripheral lesion as one of periaxial or segmentary neuritis, meaning by that term inflammation only of the medullary sheath of the nerve, for the axis cylinder is spared; hence their explanation of the early recovery of the loss of motion in some cases of saturnine paralysis. As this segmentary neuritis is found in a large number of infectious and inflammatory diseases, its value in lead poisoning is for that reason much discounted. In a disease like plumbism, where paralytic phenomena quickly develop, and occasionally, though very seldom, just as rapidly disappear, the probability is that the central nervous system and not the peripheral is to blame. At any rate the spinal cord is not always healthy. Déjerine found changes in the anterior roots, similar to those observed in the peripheral nerves, and in cases of acute lead poisoning that exhibited paralytic phenomena, there has sometimes been found marked hyperæmia of the anterior cornua of grey matter of the spinal cord. The large multipolar cells in the spinal grey matter are probably so affected by the toxæmic blood in plumbism, that they fail during life to transform and transmit impulses, without exhibiting after death any noticeable alteration of structure. In experimental plumbism I have failed to detect evidence of peripheral neuritis in the paralysed limbs of animals. My feeling, therefore, is to regard the ganglion cells in the spinal cord as primarily affected, and as a consequence of the slight and unrecognisable changes of structures therein established, the peripheral terminations of nerves, which are the most vulnerable, because they are furthest removed from their trophic centres, either become secondarily affected or fall a readier prey to the action of the toxic blood. Fisher of New York found central as well as peripheral nerve changes in the body of a painter who had suffered from repeated attacks of colic, whose hands were paralysed, and who died after an epileptiform seizure. The peripheral nerves were degenerated, and the cord in its upper dorsal region showed atrophy of the anterior cornu on one side, and the antero-lateral tract of

the other, along with sclerosis of Goll's column. Pal maintains that the cells in the anterior cornua may be affected in plumbism, without any marked degeneration observable in the nerve fibre. Onuf reported the case of a painter, æt. 37, who had suffered from colic, paraplegia, paralysis of flexors and extensors of left arm. At the autopsy, poliomyelitis of the anterior cornua of spinal cord, infiltration of the arterioles of the cord with small round cells, degenerated anterior roots, and increase of interstitial tissue of the plantar nerve, were found. There is a history of traumatism in the case, which weakens the value of the report. Nissl, Lugaro, and Marinesco found both in lead and arsenical poisoning that the multipolar cells in the anterior cornua of the spinal cord were altered: (1) There was a disappearance of the stainable substance of Nissl from the dendrites or from the cell body; (2) on the dendrites were nodular swellings, corresponding to accumulations of stainable substance; (3) a tendency to disorganisation of individual Nissl bodies, especially at the periphery of the cell. Kussmaul and Maier found hypertrophy and sclerosis of the connective tissue of the sympathetic ganglia, particularly the cœliac and upper cervical, along with induration and a decrease in the cellular elements of these organs, as a consequence of chronic plumbism.

Individuals who have suffered for years from lead poisoning become old prematurely. If they have escaped the paralysis and blindness already alluded to, they are observed to be extremely cachectic and ill-nourished. The face is swollen in the morning, at night their feet are œdematous, the urine contains albumin; they suffer from shortness of breath, and they either die in uræmic convulsions or from subacute inflammation of the lungs. At the autopsy the left heart is found to be hypertrophied; there is aortic valvulitis with fibrotic arteries; the liver is shrunken and cirrhotic, the kidneys contracted and their capsule adherent. It is the kidneys of these chronic cases that are the seat of advanced interstitial nephritis. In consequence of the cardio-vascular and renal changes, the brain may be the seat of hæmorrhages.

Sooner or later, as already stated, the kidneys become affected, and albumin appears in the urine. It is probably in consequence of failure on the part of the eliminating organs that many of the severe nervous symptoms arise. As a rule, in the early stages of plumbism there is no albumin in the urine, but old lead workers pass a urine which is pale and watery, has a low specific gravity, contains albumin, and has all the physical and chemical characters observed in cases of chronic contracting kidney. Occasionally there is hæmato-porphyrinuria. The urine, which may be light-coloured on being passed, becomes on standing cherry-red, then like light port wine, and ultimately very black. On adding to it a small quantity of hydrochloric acid in the cold, the urine gives the spectrum of hæmatoporphyrin, namely, one band in the red, one in the green, and another to the right in the ultra-violet.

Symptoms.—Abdominal colic is one of the earliest symptoms. Usually before abdominal pain is complained of, the face has been observed to be paler, and the patient has been conscious of an increasing disinclination for food, and of a disagreeable taste in the mouth in the morning. As a rule the colic is severe and recurrent, and is frequently associated with a hardened and retracted state of the abdomen, due to reflex spasm of the parietal muscles. The pain is referred to the neighbourhood of the umbilicus, or it is diffused over the upper two-thirds of the abdomen, and is accompanied by sickness. Usually there is obstinate

constipation, but there may be diarrhœa. Even after the bowels have been freely opened by aperients, colic continues, clearly indicating that the pain is not altogether due to constipation. Pressure upon the abdomen sometimes aggravates, sometimes it relieves, the pain. Some patients obtain relief by firmly pressing their abdomen, whilst by others even gentle pressure cannot be borne. It is one of the features of lead colic that in many cases the pain is confined to one-half of the abdomen, or it is worse in one-half than the other, and that pressure aggravates it. Associated with this one-sided location of colic, I have frequently noticed that considerable pain is also experienced when firm pressure is applied to the corresponding side of the neck along the course of the pneumogastric nerve, a little above the sterno-clavicular articulation. As the colic and vomiting subside and desire for food returns, it is observed that the unilateral colic and pain in the neck disappear concurrently. The pupils are frequently unequal, the pupil on the same side as the abdominal pain being usually, but not invariably, the smaller. The pulses at the wrist are unequal, the pulse on the same side as the colic being sometimes stronger, sometimes weaker, than the other. What colic is really due to it is difficult to say, but there is evidently spasm of certain portions of the small intestine, caused by the direct action of lead upon the muscular fibres of the intestine, the musculature of the intestinal arteries, or upon the nerve ganglia and their connections. Although colic is one of the most common symptoms of lead poisoning, it is well to remember that it may never appear during the whole course of plumbism. An interesting phenomenon observed in lead colic is the occasional disappearance of sulphocyanide of potassium from the saliva, and its return on subsidence of the pain.

Mouth.—In old lead workers the gums are ulcerated. Nearly all patients exhibit a well-marked blue line close to the margin of the gums and teeth, a physical sign of considerable diagnostic importance, but often absent in young subjects whose gums are sound and whose teeth are kept clean by brushing. For its development it is necessary there should be some slight space between the gums and the teeth wherein decomposition of albuminous food may take place. This line is due to a deposit of sulphide of lead in the deeper epithelial and connective tissue cells of the gum close to the papillæ, and does not depend, as some have taught, upon embolic plugging of the small blood vessels of the gum by particles of sulphide of lead. Once developed, this blue line, first described by Burton, may persist for months in spite of treatment. I have seen it disappear in from two weeks to four months. In lead workers sometimes a large blue-black patch can be seen inside the lower lip. The surface of the tongue, too, may be similarly discoloured and its papillæ prominent.

Circulation.—The pulse is frequently so small during the attack, that it can scarcely be felt by the finger or even registered by the sphygmograph, but occasionally it is hard and resistant, indicating the coexistence of heightened arterial tension and abdominal pain. Accompanying the colic there is a marked fall in the secretion of urine, 4 to 8 oz. only being secreted per diem; but beyond being scanty it is usually healthy, in first attacks particularly. The pulse rate may fall to forty in the minute.

Blood.—The blood-making powers of a patient suffering from plumbism are impaired. The red blood cells are numerically deficient; the thyroid gland is occasionally reduced in size. As lead is frequently present in the bones, the hæmatogenic function of bone marrow tends to become impaired.

Females suffer from irregular menstruation. As a rule, the menstrual loss is too frequent and too profuse, but in a few cases there is amenorrhœa. Abortion is of common occurrence in female lead workers, and also in the lower animals that are the subjects of experimental plumbism. Two illustrations will suffice. One of my Infirmary patients, a woman æt. 35, had four children at full time, healthy, and who survived. She then went to a white-lead factory, where she worked for six years. During this period she had nine miscarriages and no living children. Another woman, æt. 34, had four children before becoming a lead worker—two afterwards, and then four miscarriages in succession. So marked is the tendency for the lead-tainted human female to miscarry, that in cases where repeated abortion has taken place, the only chance of such a woman ever reaching the normal term of pregnancy and bringing forth a living child depends upon her leaving the white-lead factory altogether. The mortality of children born under these circumstances is high; most of them die shortly after birth from convulsions. If a child is born alive to parents who are both lead workers, it is puny and ill-nourished, and generally dies a few days after birth. In such infants I have found the liver, on microscopical examination, the seat of an intercellular cirrhosis, and on chemical analysis the organ contained lead. When I have administered lead to pregnant rabbits, the metallic poison has subsequently been found in the fœtuses, clearly indicating the ease with which lead traverses the placenta. In the human as in the lower animals, it may be owing to death of the fœtus as much as to any special action of the poison upon the uterus, that abortion so readily occurs. Lead is a strong ecbolic, and is occasionally resorted to by women in the form of diachylon pills, as an abortifacient, with direful results.

Cerebral.—Headache, usually severe, is a common symptom. In acute plumbism, headache may be a premonition of impending convulsions. There may be a succession of epileptiform seizures, accompanied by loss of consciousness, during which the patient may die. This is the most serious form of acute plumbism, and to it the term "lead encephalopathy" is applied. As a rule, convulsions are preceded by such symptoms as headache, diplopia, colic, and wrist-drop, but these may supervene without any premonitory warning beyond headache. Occasionally, young women who are the victims of lead poisoning are observed to become changed in their manner; they complain of severe headache, and become hysterical. Such a combination of symptoms may throw medical men off their guard. Too often this toxic hysteria foretells the advent of epileptiform seizures, which may prove fatal within forty-eight hours. When the convulsions subside, the patient may remain restless and delirious for a time, and subsequently become melancholic, the spell of which may be broken by recurrent mania. One of the most distressing sequelæ of saturnine epilepsy is blindness. The loss of sight may be complete and permanent. In a few cases vision may be regained, even after a lapse of several weeks.

A rare form of paralysis due to lead is hemiplegia, with or without hemianæsthesia. I have reported the case of a man who had right hemiplegia and aphasia, but in Da Costa's patient, a female who had been exposed to the odour of fresh paint, hemiplegia without anæsthesia developed in three days, preceded by severe headache, but no colic.

Symptoms similar to those of general paralysis are met with in lead poisoning. Many years ago, Tancquerel noticed a peculiar embarrassment of speech, but it was left for Delasiuive to demonstrate its relation to

saturnine poisoning, and for Parelle to describe the group of symptoms. Saturnine pseudo-general paralysis is a disease which affects males, females being exempt. The most susceptible age is from 40 to 50. It develops suddenly, being usually ushered in by delirium or an epileptiform seizure. Once the illness is fully developed, there are depression of spirits amounting to melancholia, insomnia, loss of memory, and muscular tremor, affecting principally the lips and tongue and causing embarrassment of speech. The patient resembles a general paralytic, and yet the illness may decline, speech and intelligence may return, and the individual ultimately recover.

Cord.—Since muscular inco-ordination sometimes occurs in plumbism, it raises the question, is there a saturnine pseudo-tabes? Saturnine tabes is mentioned by Gowers; it has been observed in America by Putnam, and in France by Teissier and Raymond. I have also met with it. The phenomena are exhibited mostly by males. Like the classic form of tabes, the inco-ordination is aggravated by closure of the eyes. There may be diplopia, loss of the muscular sense, incontinence of urine, and, as in Gowers' case, loss of the knee-jerk, without any affection of sensibility, and without the patient ever having had colic. Since patients thus afflicted usually improve rapidly under treatment, this circumstance has suggested that we are dealing with only a functional derangement of the nervous system; but in a fatal case, described by Morris of Charlestown, there was degeneration of the postero-lateral columns of the spinal cord. In addition to the above, I have met with saturnine ataxia in young male lead workers, where, besides muscular inco-ordination and diplopia, there were nystagmus and exaggerated knee-jerks, all of which rapidly disappeared under treatment.

Lead poisoning may cause insanity. After working in a white-lead factory for a few months, a woman may become suddenly insensible, and pass into a state of coma which lasts for a few days, its continuance being occasionally interrupted by an epileptiform seizure. On regaining consciousness, there may be complaint of colic or of headache, double "wrist-drop" may be noticed, and the presence of albumin in the urine confirmed. Without further warning, symptoms of acute mania arise, and on their subsidence the patient is for a time gloomy and despondent. There may be no fresh development, except complaint of constant headache—pains of a neuralgic character—there being several tender spots detected on pressing the nerves as they escape from the cranial foramina, and then quite unexpectedly there is a recurrence of mania, the temperature suddenly rises, it may be, to 106°, when the patient dies.

Peripheral nerves.—After working for years in a lead factory, and having experienced only recurrent attacks of mild abdominal pain which has yielded to aperients, an individual gradually or suddenly loses the power in his hands—he cannot hold things as he used to; his hands fall powerless by his side, owing to paralysis of the extensor muscles of the wrists and fingers. This "wrist-drop" is usually double, but one hand may be more affected than the other. Bilateral distribution of the paralysis is characteristic of metallic poisoning, particularly of plumbism. Once wrist-drop develops, the loss of power is followed by muscular atrophy, which rapidly progresses. The lower part of the forearm becomes flattened. The hands lie flaccid, and are flail-like in their movement; the interosseous grooves deepen, and the thenar and hypothenar eminences become flat. When the patient attempts to extend his fingers, considerable tremor

of the hands and forearms is induced, with synergetic movement of the flexor muscles. The flexors of the fingers, while weakened, are not paralysed. The supinator longus generally escapes, and thus a certain amount of movement at the wrist is still possible. Occasionally the paralysis involves the muscles of the upper arm, and in this form the supinator longus may be affected. The deltoid, biceps, brachialis anticus, and supinator longus muscles constitute what is known as the Duchenne-Erb group, and when these are paralysed it usually indicates rather a severe type of lead poisoning. Paralysis of this group of muscles generally follows where loss of power has previously been noticed in the extensors of the forearm, but it may arise independently. The deltoid is the first to suffer, and yet, though paralysed, it is still responsive to electrical stimulation. The muscles of the trunk and limbs may be also involved, so that, as the patient is unable to turn in bed, he lies completely helpless. Pain is commensurate in its distribution with the loss of power, and as the muscular atrophy makes rapid strides, the symptoms are not unlike those met with in multiple neuritis, except that in many cases the knee-jerks are exaggerated. Paralysis may creep onwards until it involves the intercostal muscles and the diaphragm, so that the patient is unable to breathe and swallow. In this type of lead poisoning, death comes from respiratory paralysis. The voluntary muscles have no sooner lost their power than they begin to atrophy. They exhibit at an early date, when tested electrically, the "reaction of degeneration"; that is to say, the muscles fail to respond to faradic stimulation, but contract to the slowly interrupted current.

In severe cases of lead paralysis affecting the forearm, a few of the muscles of the leg may be also involved, constituting the peroneal type of the disease, the interesting point being that, while the long extensor of the toes and the peronei muscles are affected, the tibialis anticus (like the supinator longus in the forearm), although supplied by the same nerve, namely, the external popliteal, escapes. Before this form of paralysis develops, there is usually considerable pain complained of in the muscles of the leg, the skin over which may be either hyperæsthetic or analgesic.

There is a form of lead poisoning in which the small muscles of the hand, *e.g.* the interossei and those of the thenar and hypothenar prominences, become affected, in which atrophy is not only well marked, but seems rather to keep pace with the paralysis than to follow it, producing a loss of power and creating a deformity closely resembling that observed in progressive muscular atrophy. It is spoken of as the Aran-Duchenne type of lead paralysis, and is said to depend upon degeneration of the multipolar cells situated in the anterior horns of the grey matter of the spinal cord, or upon a gradual wasting of nerve fibres and muscles. It resembles progressive muscular atrophy in so far as there is a diminution of irritability to both forms of electricity present from the first, and which gradually increases, there never having been a period of lost faradic and preserved voltaic excitability. This form of paralysis is extremely slow in disappearing, and complete recovery is but seldom. One of the best illustrations of this form of paralysis I have seen was in a plumber in whom only the small muscles of the hands were affected. The extensors of the wrists, although weakened, were not paralysed. The appearance of the hands exactly resembled that observed in progressive muscular atrophy. There was no loss of sensation. I have observed the same form of paralysis in the file-cutters at Rainhill. Those muscles are worst which, as Möbius showed,

are preponderatingly used in particular occupations. The plumber just alluded to showed another interesting fact, namely, the greater ease with which extension of the wrists could be accomplished when the hand was flexed, also the fingers flexed upon the palm.

The paralytic phenomena of double wrist-drop are usually slow in disappearing, even under treatment, and at the best recovery is often incomplete. Sensation over the affected muscles is generally normal, but occasionally the skin is analgesic, the prick of a pin not being felt. This loss of sensation is frequently observed on the back of the forearm. When the skin is pricked, blood is drawn, a circumstance which shows that the condition is not one of hysterical anæsthesia. As a rule, lead paralysis develops without fever, but Bury, quoting Meignen, alludes to a generalised form of paralysis, occurring with pyrexia, and attended by symptoms such as at first suggested typhoid fever or subacute spinal paralysis.

Eye.—As stated higher up, blindness may be a sequel of saturnine epilepsy, but it may arise apart from it. Three forms of loss of sight are met with in plumbism. In one, the blindness, which has rather suddenly developed, accompanies headache. Complete or incomplete, this form is always transient, and is evidently due to a toxæmic condition of the central or deeper parts of the brain concerned in vision, or upon an anæsthetic state of the retina, for, on ophthalmoscopic examination, the disc and retina are found to be normal. Besides, the loss of sight is intermittent; vision may at any time return. In other patients the loss of sight is absolute and enduring. There may have been colic and severe headache protracted over a period of days, or there may have been encephalopathy, antecedent to the loss of vision. The patient is perhaps young, and otherwise healthy, and the urine is free from the presence of albumin. On ophthalmoscopic examination, the discs are observed to be swollen, and to have ill-defined and irregular borders; there is distinct hyperæmia with mottling, or the arterioles are small and obscured, the venules being distended. In addition, small hæmorrhages may be observed close to the border of the disc or in the retina. Subsequently the disc atrophies, and becomes extremely pale. The sight is sometimes partially restored — usually it remains permanently lost. This is the form of neuro-retinitis met with in acute plumbism. It differs from that subsequently to be mentioned, and which occurs in chronic forms, accompanied by kidney disease and albuminuria.

Bell Taylor mentions a case of saturnine amblyopia, limited to one eye, occurring in a young woman who took diachylon, 10 grs. nightly for three weeks, to induce abortion. There was white atrophy of the left optic disc, and marked central scotoma in both eyes (amblyopia without tissue change). The right eye recovered perfectly under treatment. It is interesting to note that, while the diachylon caused blindness in one eye, there were never any signs of plumbism, such as colic, blue line on the gums, nor paralysis. Diplopia and nystagmus are occasionally observed in lead poisoning, also loss of colour perception, particularly for yellow and blue.

Parotid gland.—Attention has been drawn by Comby of the Sick Children's Hospital, Paris, to a form of toxic parotiditis occurring in lead workers. Usually the glands on either side of and behind the jaw are swollen and painless. The patient looks as if he had mumps. The disease occurs at any age, but there has generally been a history of colic and albuminuria, and occasionally of painful enlargement of the testicle. Thieleman in his thesis

upon this subject reports thirty cases of saturnine parotiditis. In some of his patients mastication was uncomfortable, and the gland was painful to the touch. He believes that the parotid enlargement is due to elimination of lead by the saliva. That lead is eliminated by the saliva has for long been known. Pouchet found it in the saliva of lead patients as long as three months after the individual had ceased working in the factory. Spillman injected pilocarpine into a patient, suffering from saturnine colic, and within four minutes he obtained 315 grms. of saliva in which he found 3 mgrms. of lead. Enlargement of the parotid gland has also been induced in saturnine patients suffering from colic, by the administration of potassium iodide. Although lead of itself may give rise to a form of parotiditis, it is more than likely that in its causation infection of the gland plays a part equally important to saturnine intoxication.

Antrum.—Maxillary sinusitis has been found by H. L. Wagner to be due to chronic lead poisoning. The symptoms were excruciating right supra-orbital pain and hyperosmia, whereby strong odours excited pain. There was hypertrophy of the lower and middle turbinated bodies on right side of nose, a sero-purulent discharge rich in micro-organisms, with crusting at the entrance of the hiatus semilunaris, and pain on pressure over the region of the first right molar tooth. There was no blue line on the gums; the man was a coachman, æt. 32. Diagnosing disease of the antrum, the hard palate was drilled and the cavity packed with borated gauze. No relief followed. No lead was found at this stage in the urine, but as the fresh scrapings of the hypertrophied tissue of the antrum gave, with sodium sulphide, a lead reaction, patient was placed upon iodide of potassium. In a few days all pain had disappeared and the discharge lessened, and shortly afterwards the patient was well. The urine, hitherto free, now exhibited a trace of lead. Wagner regarded the diseased condition of the antrum, including the neuritis of adjacent nerves, as due to the deposit of lead, probably in the form of albuminate.

Testicle.—Orchitis is said to be caused by lead. I have only met with it once in a lead worker, and where all other causes could be excluded.

Gout.—Plumbism and gout are correlated. The association of the two diseases is not so close, however, as some maintain. In the north of England and in Scotland, gout is not a common disease, and as a symptom of lead poisoning it hardly ever occurs. In London and the south it is just the reverse. Climate, the drinking habits, and the nature of the food of the people, may have much to do in explaining this difference. Whisky is the drink of the North and beer of the South, and it is admitted that beer of itself tends to develop uratosis. From my experience of gout and lead poisoning, I am of opinion that in nearly every instance in which gout has arisen in an individual suffering from lead poisoning, it has been due to a hereditary predisposition to gout, and in this opinion I am supported by Ebstein, who, in describing the ailments of the lead workers on the Harz Mountains, has come to a similar conclusion, namely, the comparative absence of gout in individuals who are free from the hereditary taint of the disease; also by Roberts, who states that both in the gouty diathesis and in plumbism the same tendency is present, namely, the deposition of crystalline urates in the tissues of the body. This vice in a lead poisoned individual, or, as Roberts calls it, saturnine uratosis, is exaggerated, if such a person is hereditarily predisposed to gout. In plumbism, the elimination both of urea and uric acid is defective. Uric

acid is apparently retained in the system, owing probably to lead circulating in the blood, reducing its alkalinity, and thereby rendering the uric acid insoluble.

Garrod found uric acid in the blood of seven out of nine persons suffering from plumbism, without any gouty symptoms. This circumstance clearly shows that lead has a tendency to cause accumulation of uric acid in the blood. Of this we have further confirmation in the fact that, when acetate of lead is administered, it is followed by a diminished elimination of uric acid in the urine. It is therefore astonishing that in Newcastle-upon-Tyne, where so much lead poisoning prevails, there should be such a marked absence of gouty complications. So rare, in fact, is the association, that five or six years will pass without a case being admitted into the infirmary; probably not once in 400 patients. In nearly every instance where I have met with gout and plumbism, the patient has been a male, usually a house painter, and his father and grandfather have followed the same occupation. It is not therefore a question simply of lead poisoning in the individual immediately causing gout, but of a constitutional peculiarity developed under the influence of lead, hereditarily transmitted, and out of which, during plumbism, the gouty state may be evolved. Luff, in his Goulstonian Lectures, has carefully dealt with this subject. He considers that the gouty paroxysm in saturnine poisoning depends rather upon functional imperfection of the renal epithelia. It is not necessary, he says, that the kidneys should be absolutely diseased, but should act imperfectly so that uric acid cannot be eliminated. While lead poisoning predisposes to gout, it is more than likely that gout also predisposes to plumbism.

That nitrogenous metabolism in lead poisoning is diminished and deranged, there is no doubt. My own observations support those of Surmont and Brunelle and Gaucher. The urea is usually diminished, but the uric acid varies, being sometimes increased, sometimes diminished. It is by deranging nutrition that lead poisoning causes gout. To induce this illness, the system must be gradually and slowly brought under the influence of the metallic poison. That is one reason why house painters suffer most from gout, while white-lead workers escape. All my patients who have had saturnine gout were house painters, and in them there was not only the history of a long exposure to lead, but also one of a hereditary influence. The disease as observed in plumbism differs in no way from ordinary gout, unless in its greater tendency to be associated with interstitial nephritis, a tendency to appear at an earlier age, usually before 35; that it develops in people not in good health, as does ordinary gout, but in those who are anæmic, reduced in health, and frequently albuminuric; that it tends to invade other joints than the big toe, and that several attacks may be experienced within a few years.

Rare as saturnine gout is in the north of England and Scotland, it is quite as uncommon in France and Germany. Ebstein did not observe any very close relationship between plumbism and gout, nor did Jacob (Lauthenthal) find gout frequent amongst the miners of the Oberharz. Opposed to this, however, we have the testimony of Luethje, that of 6000 workmen 800 were employed in that particular part of the factory where silver is extracted from the lead ore. These were therefore exposed to plumbic emanations, the proportion of men employed being thirteen miners to two silver extractors. During eight years he found that 217 miners suffered from gout, also 103 of the men engaged in the desilvering

processes; that is, one case of gout in twenty-four miners for one in eight silver workers. It would be interesting to know the drinking habits of the two classes of workmen, and to what extent, if any, their food differed.

Diagnosis.—As a rule, the diagnosis of acute lead poisoning is easy. The history of the case, the sudden development and severity of the colic, the extreme restlessness of the patient, previous complaint of metallic taste in the mouth, and the presence of a blue line on the gums, all testify to lead being the cause of the illness. The difficulty of diagnosis arises in cases where there is no blue line on the gums, no history of the individual having come into contact with lead, and where the health has been simply gradually undermined. A slowly developing cachexia with a sense of malaise, recurrent abdominal pain, a history of menorrhagia, or repeated miscarriages if a female, great debility, mental depression, and constipation, accompanied by a disagreeable taste in the mouth, occurring in an individual whose organs are otherwise healthy, should oblige us to examine the urine for traces of lead, and particularly so if, in addition to the above, there is an ill-defined or limited paralysis. The presence of lead in the urine is not absolute proof of chronic lead poisoning. Como and Worcester examined the urine of 150 persons living in Boston, and found lead in 25 per cent. In none of these people were there signs of plumbism. Bilateral paralysis is extremely suggestive of plumbism. It might be mistaken for alcoholic neuritis, but although pain in the muscles is also complained of in lead poisoning, there is less tenderness in them when grasped by the hand than in early alcoholic paralysis; in plumbism, too, the loss of power affects rather the muscles of the upper than the lower extremities. This circumstance tends to differentiate it also from arsenical paralysis, where the muscles that are affected are those that flex the ankle and extend the toes. Paralysis from pressure upon the musculo-spinal nerve is unilateral, that from plumbism is bilateral. Apart from the history of the case, it is difficult to diagnose the convulsive seizures of lead encephalopathy from ordinary epilepsy or uræmia, but the presence of a blue line on the gums and albumin in the urine would be a guide.

Chemical tests for lead.—Since lead is a subtle poison and is eliminated by the kidneys, the detection of the metal in the urine of a patient would, other symptoms being present, pretty conclusively point to the illness being lead poisoning. The examination is made as follows: Evaporate 50 c.c. or 2 oz. of urine to dryness; ignite the residue, extract the lead from this by means of sulphuretted hydrogen or ammonium sulphide. The objections to this procedure are its tediousness, and the necessity for the preliminary destruction of organic matter. In Abram and Marsden's method, a strip of magnesium is placed in the fluid to be examined. Ammonium oxalate, in the proportion of 1 grm. to 150 c.c., is added. If lead is present, it is deposited on the magnesium. A deposit is seen within half an hour, but it may require a longer exposure. The slip is then washed with distilled water, and dried. To confirm the test— (1) Warm the slip with a crystal of iodine upon it—a yellow colour proves the existence of lead; (2) dissolve the deposit in nitric acid, and apply the usual tests for lead. This is an extremely delicate test; it is capable of detecting 1 part of lead in 50,000, whether the metal is dissolved in water or is contained in an organic liquid like urine. It is difficult to say for how long lead will be eliminated by the urine, but in a case of acute lead poisoning Zinn found the metal twenty-five days afterwards. Lead also leaves the body by the fæces.

Prognosis.—In the minor forms of plumbism the prognosis is favourable. The mortality of lead colic is less than 2 per cent. Recovery from lead paralysis is variable, both as regards rapidity and completeness. Once an individual has suffered, he should be removed from all possible chances of contact with the poison. In patients who are cachectic, who have had repeated attacks of colic, and whose urine is albuminous, the prognosis is unfavourable. Under all circumstances, lead encephalopathy is serious, not only at the time, but on account of such sequelæ as blindness and melancholia.

Treatment.—The treatment of plumbism is preventive and curative. If the illness depends upon the use of contaminated drinking-water, care should be taken to remove from it all organic impurities, such as nitrates and nitrites, to neutralise acidity if present, get rid of carbonic acid by exposure, to harden the water (if soft) by adding limestone or by passing it through fine sand, to substitute glass-lined or iron pipes for those made of lead, to avoid the storage of drinking-water in lead cisterns, and to have water for all purposes of cooking and drinking carried into the houses direct from the main by iron pipes, and that, where water has lain in the pipes of a house overnight, to allow it to run to waste in the morning for a few minutes before using it. Thresh speaks favourably of galvanised iron pipes, since even if the zinc is acted upon by the water, zinc is not, like lead, a cumulative poison. For lead workers in white-lead factories, regulations are now in force which will tend to minimise but not remove the risk to health. By attention to cleanliness and the use of sulphur baths, plumbism may be largely avoided. The curative part of the treatment divides itself into that for (1) colic and its accompaniments, (2) paralysis, (3) encephalopathy, and (4) the deteriorated health of chronic plumbism.

For constipation and mild colic, a gentle aperient, *e.g.* Epsom salts or castor-oil, may be sufficient, but the pain may be so great that, in addition to the above, opiates or belladonna may be necessary, or a hypodermic injection of morphine. Should constipation, colic, and vomiting continue, enemata may be called for, and the administration of effervescing mixtures along with the application of belladonna fomentations to the abdomen. If these measures fail, colic can generally be relieved by a warm bath. A mixture of potassium iodide, magnesium sulphate, and tincture of belladonna is usually sufficient both as an aperient and calmative. Combemale finds large doses of olive oil very useful in relieving colic; and, should the oil be vomited, then 3 grs. of menthol administered before the next dose of oil will allay the sickness. Experience has led me to regard monosulphite of soda in 5 to 10 gr. doses, or more, thrice daily, as a good calmative for colic and as an eliminator of lead. Potassium iodide is generally regarded as the best eliminant of lead. It must be used with caution, however, for there are cases on record which support the theory, propounded by Melsens, that in a quiescent case of plumbism alarming symptoms may suddenly develop, under the administration of potassium iodide, owing to the drug rendering soluble, and therefore absorbable into the circulation, lead which had been deposited in the tissues, and was inert.

For saturnine paralysis the application of electricity and the employment of massage, combined with the internal administration of potassium iodide and nux vomica, or the subcutaneous injection of liq. strychninæ, are useful. The application of electricity, while the patient is in an acidulated bath, as recommended by Semmola and alluded to by Yeo, is said to have

been followed by a rapid elimination of lead from the system, as evidenced by the blue line quickly disappearing from the gums, and the increasing quantities of lead found in the urine. The question of the elimination of lead by electricity from the system of a lead-poisoned individual has lately been revived. It was an old belief that lead and mercury could be extracted from patients' bodies by electricity, but there is nothing to confirm this statement. Lewis Jones has employed alternating currents with great success. Electrolysis can play no part in the result, for this is rather the property of the direct current. Electricity, by stimulating nerve and muscle, and by improving the circulation, favours elimination by natural methods. Jones recommends an arm bath of stoneware filled with warm water. Into this the forearms and hands of the patient are inserted, and an electrical current passed from one end of the bath to the other. It is here the electrodes are placed. The alternating current obtainable from the electric light main of 100 volts is reduced by a transformer to 12, 14, or 16 volts, to suit each individual case. Experience shows that, although paralysed muscles do not contract to alternating currents, they are still favourably influenced by them and recovery hastened. For patients belonging to the wealthier classes, and whose circumstances allow of them visiting Continental spas, the waters of Carlsbad and of Brides-les-Bains are highly recommended.

For the convulsive seizures of lead encephalopathy the inhalation of nitrite of amyl often cuts short the attack, and, where there is suppression of urine, relief will follow the hypodermic injection of pilocarpine. In some cases venesection might become necessary, followed by saline transfusion.

As regards those cases of chronic plumbism with cachexia and signs of impaired general health, attention to the diet, which should be largely milk, regulation of the bowels, prevention of cold, abstinence from alcohol, and the internal administration of syr. ferri iodidi, or tabloids of bone marrow, may do much to prolong life. At this stage, however, treatment must be more or less symptomatic.

LEAD POISONING IN CHILDREN.

Symptoms.—Allusion has been made to contaminated drinking water as one of the commonest causes of accidental plumbism. In the Colonies, where water is sometimes scarce, and has to be stored for lengthened periods in galvanised-iron tanks, Jefferis Turner and Lockhart Gibson have succeeded in tracing obscure forms of nervous disease in children to this source. In the manufacture of galvanised-iron tanks, it has frequently been found that the molten zinc into which the iron tanks have been dipped in order to become galvanized, contains lead. Some of this becomes dissolved in the water which lies undisturbed in the tank during long spells of dry weather. The government analyst of Queensland found lead in sufficient quantity to be harmful, in the water which had lain for some time in galvanised-iron tanks. In Brisbane, children suffered from headache and vomiting, followed by paralysis of the ocular muscles, and by blindness, symptoms which at first suggested meningitis rather than poisoning. Jefferis Turner and Lockhart Gibson, after carefully unravelling all the facts, succeeded in differentiating the cases, and placing them in their proper category. In adults, plumbic paralysis as a rule appears first in the extensors of the wrists and fingers, but in children of tender years "foot drop" is usually one of the earliest nervous manifesta-

tions of lead poisoning, the muscles affected being the tibialis anticus and the extensor longus digitorum; sometimes, too, the peronei. Later on, in advanced cases there may be weakness and altered electrical reaction of the calf muscles, spasm of these muscles, and persistent talipes equinus. Should the arms become affected, the extensors of the fingers are the first to become paralysed, those of the wrist only when the illness is more pronounced. The short muscles that form the ball of the thumb may also become paretic and wasted, the adductor pollicis, however, being less liable to be thus affected than the abductor opponens and flexor brevis. The interossei do not exhibit in children the same tendency to become paralysed as in adults. Turner saw two patients in whom there was paralysis of the diaphragm. In the paper from which I have quoted, Turner lays considerable stress upon the fact of paralysis from lead poisoning in children occurring first in the feet and legs, as opposed to the wrists, and in this he is supported by the experience of J. J. Putnam, who found in every instance the legs affected as much if not more than the arms, and that the paralysis had always appeared first in the lower extremities, just as in arsenical and alcoholic poisoning. As in adults, so in children, the development of paralysis is often preceded by "bilious attacks," recurring every few months, during which there is acute abdominal pain, the bowels being usually, but not invariably, constipated, for occasionally there is diarrhœa. A blue line may be present in the gums, but this as a physical sign is oftener absent in children than in adults, owing probably to the smaller amount of nitrogenous food they consume, and the fact that the teeth in young children seldom collect tartar. Once the colic is recurrent, it may be followed by pains in the muscles of the legs, and by paralysis and convulsions. If a patient has had convulsions, it is observed, on his regaining consciousness, that there is paralysis of some of the ocular muscles, usually the external rectus, that the face is slightly paralysed, that the head is retracted, and that the child is blind. On ophthalmoscopic examination, there is found double optic neuritis, the discs are swollen, there is exudation into and around them, the veins are tortuous and distended, and small hæmorrhages here and there are observed in the retinæ. By degrees these signs subside, and the discs are noticed to be pale and passing into a condition of post-neuritic atrophy. In the lead poisoning of children, one of the distinguishing features is, that while there is a marked tendency for optic neuritis to develop, it is much more frequently associated with oculo-motor paralysis than in adults. Occasionally the course of the illness is broken by febrile attacks, which last for a few days, and the cause of which is rather obscure. The face begins to wear a pained expression, the skin becomes pale and swarthy, and the urine, while it may or may not show a distinct trace of albumin, almost invariably, on careful chemical analysis, is found to contain a minute quantity of lead.

It is difficult to say to what extent children, compared to adults, suffer from plumbism in endemic lead poisoning. John Brown of Bacup had the opportunity of investigating 303 cases of lead poisoning which occurred in one year in his district, and he gives us the following:—

Under 1 year . . = 5 cases.	15 years and under 25 years = 68 cases.
5 years and under 10 years = 18 ,,	25 ,, ,, 50 ,, = 144 ,,
10 ,, ,, 15 ,, = 20 ,,	50 ,, upwards . = 48 ,,

Brown found in this epidemic that lead poisoning occurred less frequently in children, a circumstance probably due to their greater eliminating powers. In Queensland, on the other hand, lead poisoning appears to

have played sad havoc with children. Taking the Brisbane Children's Hospital alone, seventy-six cases of plumbism were admitted in six years, and of these seven died. In all probability the cases in private practice were just as numerous. No age of childhood seemed to be exempt after the first year, but the ages of 5, 6, and 7 seemed to be the most vulnerable, for these years furnished 71 per cent. of the total cases. It is interesting, too, to note that even at this early age females showed a greater susceptibility to lead poisoning than males: 72 per cent. of the patients were girls. Although all the children in the family were drinking the same water, the poison affected only one or two of the most susceptible. Turner, as the result of his experience, believes that children are more susceptible to plumbism than adults, and he lends considerable weight to the opinion I have always expressed, namely, the greater susceptibility of the female sex. Children of a gouty father are specially prone to suffer.

Diagnosis.—A history of recurrent headache, bilious vomiting, and abdominal pain, presence of a blue line on the gums (oftener absent, however, than present), paralysis of various muscles, the loss of power, appearing first in the leg and foot, and subsequently involving the fingers and wrists, preceded by tenderness, and followed by wasting, are of themselves extremely suggestive of lead poisoning. Add to these symptoms—convulsions, followed by oculo-motor paralysis, usually of the external rectus, facial paralysis, retracted head, stiffness of the neck, and changes in the optic disc; and while there is in these symptoms much to suggest a basal meningitis, the presence of lead in the drinking water, the detection of a trace of lead in the urine, the fact that muscular paralysis and disc changes are frequently simultaneous, that the disc changes are sometimes unilateral and on the side opposite to the paralysed external rectus, also that in cases where there has only been optic neuritis the patients have recovered, and we have a congeries of signs and symptoms pointing pretty conclusively to lead poisoning.

Treatment.—The treatment of lead poisoning in children is practically the same as for adults. If due to drinking water, remove the patient from his home, and discontinue the use of the contaminated water; allow him no sweetmeats that are artificially coloured; promote elimination by gentle action upon the bowels by saline aperients, by diaphoretics, such as the subcutaneous injection of pilocarpine, followed up by the internal administration of potassium iodide, carefully the while watching its effects.

ARSENICAL POISONING.

POISONING by an overdose of arsenic, or arsenious acid and its compounds, administered accidentally, suicidally, or with criminal intention. Arsenic causes few deaths either accidentally or suicidally, but criminally the number is large. During five years ending 1890, seventeen fatal cases of arsenical poisoning occurred, of which twelve were males and five females, whilst during the quinquennium ending 1895, arsenic caused sixty-four deaths. By the term white arsenic we mean arsenious acid.

History and etiology.—The poisonous properties of arsenic have long been known. Its comparative tastelessness is one reason why it has been so frequently resorted to for criminal purposes. Metallic arsenic is

harmless. It is only when it is brought into contact with the juices of the animal body, or is volatilised, that it assumes highly poisonous properties. Arsenical compounds cause poisoning, whether they enter the system by inhalation, are swallowed with the food, or are applied externally to the skin. It is owing to the escharotic properties of white arsenic that it was formerly used in the surgical treatment of cancer. As the active ingredient of a paste applied to cancer, it is known to have caused death. Men who are employed in smelting zinc frequently suffer from symptoms of arsenical poisoning, owing to the presence of arsenic in spelter. Cobalt miners are similarly affected; so also are workmen who are engaged in the manufacture of emerald-green. Arsenic is largely employed as a medicine in the form of Fowler's solution, or liquor arsenicalis, which is a 1 per cent. solution, with an alkaline reaction, composed of arsenite and carbonate of potassium and coloured by sandal wood. In small doses, Fowler's solution is a valuable remedy, but its administration requires care. Of late it has been given rather freely in the treatment of chorea, and has caused bronzing of the skin, gastro-intestinal irritation, and paralysis, which have gradually disappeared on discontinuing the medicine. A few years ago arsenic was frequently present as a pigment in wall papers. People occupying rooms thus lined frequently suffered from great depression of spirits, nausea, vomiting, irregular stools, headache, dry throat, laryngeal and bronchial catarrh, reddened eyelids, symptoms suggestive of a severe cold in the head, whilst others suffered from gastritis. The detection of arsenite of copper in wall paper and the experiments performed by Kramer in 1852, with the view of determining how far volatile arsenical compounds could be liberated under these circumstances, confirmed the suspicion of the symptoms being due to arsenical poisoning. Previous to this, Basedow had in 1846 drawn attention to poisoning arising from wall-paper, and in 1848 he succeeded in getting the Prussian Government to make penal the addition of arsenic to wall paper. It is now generally admitted that illness may be caused by the inhalation of arsenical dust, arseniuretted hydrogen, or arsine, arising from the action of arsenious acid upon organic matter. Gosio and Sanger have shown that volatile arsenical compounds are formed by the operation of certain moulds upon organic matter containing arsenic, and that in the growth of these moulds an intense garlicky odour, characteristic of arsenic, is evolved. Saccardo found in decaying paper, one mould, the *Penicillium brevicaule*, which is so sensitive to the presence of arsenic, that Gosio utilises it as one means for detecting arsenic in toxicological preparations. Other micro-organisms may be similarly endowed, but there are four arsenio-bacteria, about whose operation there is no doubt, and these are the *Penicillium brevicaule, Mucor mucedo, Aspergillum glaucum,* and *Aspergillum virens.* Experiments with these moulds show that a gaseous or volatile compound is generated from decaying arsenical matter.

Although arsenic is poisonous to all forms of animal life, it can yet be taken for a lengthened period, and with considerable impunity, provided small doses are commenced with. There is some truth in the arsenic eating powers of the Styrian peasantry, and their immunity from the disastrous consequences usually observed in cases where the drug has been administered rather freely. Anything above two grains of arsenious acid must be regarded as a dangerous dose.

Morbid anatomy.—In acute cases, pathological changes are observed

in the stomach and intestines. The mucous membrane is swollen and congested, and is the seat of numerous small ecchymoses or emphysematous bullæ. It may be covered with a diphtheritic exudation. So persistent is the inflammatory redness of the stomach and intestines, that a few months after a person has died from arsenical poisoning, the coloration may still be recognised, owing to the preservative powers of the drug. At times the redness extends the whole length of the alimentary canal, and resembles that observed in cholera, a likeness which microscopical examination may strengthen, owing to the micro-organisms described by Klebs as characteristic of cholera being found in the epithelial flakes. Peyer's patches and the solitary glands may be swollen. Arsenic has such a selective influence for the lining membrane of the stomach, that, quite irrespective of the channel by which it gains entrance into the system, it is eliminated by the mucous membrane of this viscus. Thus is explained the anomalous behaviour of the poison, that in order to prove fatal a larger quantity has to be injected into a vein than when taken by the mouth. From the blood it is eliminated by the gastric mucous membrane, and in its passage outwards it acts as an irritant, causing inflammatory redness. The cells of the liver and kidneys, and the fibres of voluntary muscle, are the seat of fatty degeneration. Salkowski states that the glycogenic function of the liver is destroyed, but in animals, the subjects of experimental arsenical poisoning, I have found that the liver always contained plenty of glycogen. Of the nature of the combinations formed by arsenic in the body it is difficult to speak with certainty. Liebig thought that it formed with albumin a stable non-putrefactive compound, while Binz and Schulz maintain that in the animal organism arsenious acid is converted by oxidation into arsenic acid, and that this latter is reduced to arsenious. Arsenic would thus be simply an oxygen carrier to the tissues, hence its stimulating influence in nutrition, where under its administration the cells of the liver and kidneys proliferate, and the bones of young animals become overgrown.

Paralysis may follow the administration of small doses of arsenic continued for a period, or after swallowing one large dose. Meirowitz reports recovery from the acute intestinal symptoms, in a man who had inadvertently swallowed 77 grs. of arsenious acid. Subsequently, he developed an ataxic gait, with loss of knee-jerks; his legs became painful, and his feet swollen. Symptoms of multiple neuritis, sensory and motor, became well marked, and yet the patient recovered. Sensory disturbance is more profound; in this circumstance and in the fact that the loss of power is usually below the knee, lies the distinction between arsenical and lead paralysis. In a doubtful case the urine should be tested for arsenic.

The use of the term, arsenical multiple neuritis, suggests that the paralysis depends upon a peripheral lesion, but proof of this is wanting. Paralysis consequent upon metallic poisoning has hitherto been regarded as due to a peripheral neuritis, but pathologists have recently rather looked to certain changes primarily occurring in the central nervous system as the explanation of the phenomena. In his experimental arsenical poisoning of dogs, Popoff found the spinal cord inflamed in the early stages; in the more chronic cases, that the small arteries of the cord were thickened, that the protoplasm of the large multipolar cells became opaque and granular, their nucleus indistinct, and that the cells subsequently became vacuolated. Myelitis and changes in the ganglion cells, similar to those just described,

have been observed by other writers. It is to be noted that during the time such a profound structural alteration was taking place in the cord, there was no tenderness experienced along the course of the nerves. In other cases where the symptoms suggested a central lesion, no pathological changes have been found; the alterations in the cells must have been purely dynamic, and not such as to be revealed microscopically. Occasionally, the peripheral nerves are the seat of neuritis, so that we must regard the nervous lesions of arsenical poisoning as both central and peripheral, the localisation of which is apparently determined by individual circumstances and predisposition. The protean nature of the symptoms observed in chronic arsenical poisoning obliges us to take this view. Raymond reports the case of a girl, 7 years of age, who, after taking arsenic for chorea, developed paralysis of the legs, followed by incontinence of urine and fæces, difficulty of swallowing, and an eschar on the back. In such a case there is much to suggest a central lesion.

Symptoms.—Arsenical poisoning is acute or chronic, according to the dose and the length of time the drug has been taken. A fairly large dose causes a burning pain in the gullet and stomach, which gradually spreads all over the abdomen; it creates a sense of constriction in the throat, and a metallic taste in the mouth. These are followed shortly afterwards by vomiting and purging, attended by considerable pain. The stools are bloody or contain large quantities of bile and flaky mucus, and are not unlike those observed in cholera. Arterial tension is lowered, and there is considerable collapse. The pulse becomes feeble and irregular; the respiration is laboured and embarrassed, on account of abdominal tenderness; thirst is excessive, and the urine is suppressed; the face becomes pinched, pale, and cyanosed, and the expression anxious. Cramp-like pains keep recurring and make the patient restless; he becomes convulsed, paralysed, or comatose, and in this condition he dies in from five to twenty hours after having taken a few grains (3–5) of arsenic. So rapid is the death, and so close the resemblance of the symptoms to those exhibited in Asiatic cholera, that were this disease epidemic at the time, and nothing ascertainable in the history of the case or surroundings to excite suspicion, a mistake might readily and pardonably be made in the diagnosis.

In subacute arsenical poisoning, as the dose has been smaller, the symptoms are correspondingly less severe and remittent. Vomiting and purging may cease, only in a few days to return again. Abdominal pain may be complained of on pressure; the patient is thirsty, and has painful swallowing; the urine is scanty, and frequently it is albuminous; the heart's sounds are feeble and irregular; face cyanosed or pale; skin clammy and exhaling a peculiar odour of arseniuretted hydrogen. There are cramps in the legs and convulsions. The intellect, as a rule, is clear to the last in slow arsenical poisoning. The symptoms are remittent, the patient rallies for a time, but the improvement is not maintained.

A single large dose of arsenic may be followed by death, or a prolonged illness supervenes, which may ultimately prove fatal. Although the symptoms at first are connected with the alimentary canal, it is ultimately on the side of the nervous system that they are most observed. Motion and sensation are affected. In nearly one-half of the patients all the extremities are affected; one-fourth are paraplegic, while in the remainder there is a limited paralysis or a hemiplegia. It is characteristic of arsenical paralysis that the loss of power is principally observed in the muscles below the knee, that the muscles rapidly atrophy, and are extremely

sensitive to pressure, also that they early exhibit the reaction of degenera-
tion, namely, an absence of response to the faradic current whilst acting
to the galvanic. The paralytic phenomena of arsenical subacute polio-
myelitis are accompanied by pain and sensory derangement, and exhibit
a tendency to recover.

In consequence of the administration of small doses of arsenic for a
lengthened period, the health of the individual is slowly deteriorated,
and other diseases are simulated. The appetite is lost, the individual
emaciates, becomes increasingly feeble, and suffers from depression of
spirits, irritability of temper, and sleeplessness; the skin becomes darker,
urine scanty, the extremities numb and paralysed. It is in such cases
that a chemical examination of the urine for arsenic may at once clinch
the diagnosis.

Diagnosis.—The diagnosis of the minor forms of arsenical poisoning
is not always easy, but, given the group of symptoms previously described,
or, if a child, the history of chorea followed by paralysis and bronzing of
the skin during treatment by Fowler's solution, then with such facts before
us we should examine the urine for traces of arsenic by such a method,
e.g. as the following:—Reduce 12 to 16 oż. of urine, by gentle evapora-
tion, to one-fourth of its bulk; add one-sixth to one-fifth of pure hydro-
chloric acid; insert a bright piece of copper foil, and boil for at least
fifteen minutes when, if arsenic is present, the copper will exhibit a greyish
stain. Further on we allude to the differential points in the diagnosis of
lead, alcoholic, and arsenical paralysis. In acute poisoning by white arsenic,
microscopical examination of the vomit may reveal the presence of small
white particles, which, when washed, dissolved in boiling water, and
allowed to cool, crystallise out as octahedra of arsenious acid. These,
when heated with charcoal and soda in a blow-pipe, evolve the garlicky
odour of arsenic.

In any case where paralysis follows acute arsenical poisoning, it is
important to remember that the loss of power may not appear until long
after the time the poison was taken, and when memory of the fact no longer
occupies a prominent place in the history that is given of the illness. On
inquiry, however, it will generally be elicited that there were gastro-in-
testinal troubles, such as vomiting and diarrhœa, which gradually subsided;
that these were followed by a condition in which the limbs were at first
enfeebled and painful, or the seat of tingling and numbness, and that
gradually the muscular weakness passed into paralysis, which either
affected the four extremities simultaneously, or, as is more usual, the legs.
When the paralysis affects the limbs, it commences at the periphery and
creeps upwards towards the trunk, the loss of power diminishing from
the periphery to the centre. The extensor muscles are usually more affected
than the flexors, and those on the anterior aspect of the thigh than the pos-
terior. In four or five weeks the paralysis reaches its height, when for
a period it remains stationary, during which the tendon reflexes are found to
be abolished, and there are observed signs of the reaction of degeneration,
diffused muscular atrophy, and loss of surface sensibility. The muscles are
painful on pressure. Occasionally anæsthesia is replaced by hyperæsthesia.
Pronounced as is the paralysis, both it and the muscular atrophy are
curable. Within a few weeks they gradually disappear, improvement
taking place first at the proximal end of the limbs and then extending
towards the periphery. It is during this period of recession that
d'Erlicki and Rybalkin observed contracted tendons in the limbs, especi-

ally of fingers and toes, and that the skin became glossy and the seat of erythematous eruptions.

Almost similar sequelæ follow subacute arsenical poisoning.   There is paralysis, loss of surface sensation, pains in the calves, muscular inco-ordination, abolished reflexes, dilated pupils, and inability to close the eyelids.   The initial gastro-enteritis may not have been so severe as that already described, but it is more persistent, and accompanied by febrile rises of temperature, conditions which ere this have suggested the probability of such a case being one of typhoid fever.   When paralysis develops in this form, it has a preference for certain groups of muscles, *e.g.* the common extensors of the toes, the tibialis anticus, the proper extensor of the big toe, the peronei, and later on the vasti interni.   It respects the gemini and soleus.   If, however, paralysis has slowly developed, it may not remain cir-cumscribed, but extend to all the extremities and involve even the muscles of the trunk.

A case reported by Mott is a good illustration of arsenical paralysis, commencing in one limb and extending.   The man was employed in a chemical factory to wash the indiarubber clothing worn by men who make "sheep dip," which is known to contain large quantities of arsenic. Unfortunately this individual was not supplied with indiarubber gloves, and as the result of the repeated immersion of his right hand in what became practically an alkaline solution of arsenic, he began to suffer, six weeks afterwards, from numbness and tingling in the fingers of the right hand, with progressive loss of power in the hand.   There was no tender-ness on pressure over the ulnar nerve, but considerable loss of sensation to pressure, heat, and cold.   There was diminished reaction to the faradic current in the muscles of both arms and hands ; no reaction of degenera-tion with the galvanic current.   Twelve months afterwards there was still the same loss of power in the right hand ; fingers and thumb were fixed and semiflexed.   There was paresis in both legs, and a tottering spastic gait, exaggerated knee-jerks, ankle-clonus, skin of right hand was smooth and glossy, pupils and discs were normal.   The sensation of the right hand had improved, but not its power of movement ; the left hand was feeble, and there was general muscular weakness.   The paralysis of the right hand, the progressive enfeeblement of the muscles of the left hand and legs, the tottering gait with exaggerated knee-jerks and ankle-clonus, indicate a degeneration of the cortical pyramidal neurons, progressive in character.   This cerebral degeneration may or may not have been due directly to arsenic, but the right hand and arm were evidently the result of a neuritis, as indicated by the glossy skin.   Probably the first effects of the poison were upon the endings of the peripheral nerves of the right hand.   Arsenic, though searched for, was never found in the urine.

In industrial poisoning by arsenic, *e.g.* in emerald-green makers, paint mixers, wall-paper and artificial-flower makers, etc., paralysis may occur. Putnam has reported twenty-five cases of arsenical poisoning due to sleep-ing in rooms the wall paper of which contained arsenic.   Most of the patients developed a polyneuritis.   Imbert-Courbeyre quotes the case of a young unmarried woman, who, finding herself pregnant, took large doses of arsenic with the view of inducing miscarriage.   In course of time she was confined of a still-born child, and shortly afterwards she herself developed paralysis, affecting motion and sensation of the legs.

In addition to paralysis, muscular atrophy, and altered sensibility, some writers mention ataxia, tremor, and epileptic convulsions, as sequelæ

of arsenical poisoning. These are also met with in chronic alcoholism. Alcoholic paralysis rarely shows itself after a debauch unless there has previously been long-continued drinking. In such cases we have rather delirium than acute gastro-intestinal troubles; the latter are more characteristic of arsenic. As differential symptoms, we might say that sensory troubles, anæsthesia and pain, are, if anything, more pronounced in arsenical than alcoholic poisoning, while loss of memory and intellectual aberration are more suggestive of alcoholic than arsenical poisoning. Alcoholic paralysis is never followed by desquamation; arsenical may be. Both poisons may cause deformities. In arsenical paralysis the small muscles of the hands and feet, the interossei and the thenar, are affected, so that the patient cannot separate or approximate his fingers and thumb; whereas in alcoholic the movements first affected are those which concern the ankles and wrists, for the paralysis affects the extensors and flexors of the feet and hands. Deformities occur in arsenical paralysis, and are met with on the fingers and toes, so that the different phalanges become immobile in flexion and extension, and the feet become arched. In alcoholic subjects, when the tendons become contracted, it is principally the muscles of the forearm and leg that are affected, and as a consequence we have fixation of the hands or feet in flexion or extension. In arsenical paralysis the deformities occur at the joints of the fingers and toes; in alcoholic, they are situated on the wrists and ankles.

Prognosis.—The minor forms of poisoning usually recover. In acute cases in which the symptoms are severe, or where the paralysis involves the respiratory muscles, the prognosis is unfavourable.

Treatment.—So long as there is arsenic in the stomach, the antidote is freshly prepared ferric hydrate, made by adding liq. ammon. fort. to liq. or tinct. ferri perchlor., taking care to add the ammonia gradually, so as not to have it in excess. Another method is by precipitating tinct. ferri perchlor. by sodæ bicarb., and filtering through a handkerchief. Ferric hydrate acts by converting the soluble arsenic in the stomach into the insoluble arseniate of iron. The stomach should be washed out if the antidote is not at hand. Once the arsenic is absorbed, neither ferric hydrate nor lavage is of any service. Treatment thereafter must be purely symptomatic. Copious draughts of water favour the elimination by the kidneys. Mucilaginous drinks, composed of white of egg, barley water, olive oil, or lime water are recommended, also castor-oil. When the cramp-like pains are severe, morphine hypodermically or by the mouth may be called for, also hot applications externally. The chronic forms of arsenical poisoning are best treated by iodide of potassium, with or without sulphate of magnesia, or some other gentle aperient. In cases of paralysis, so soon as all sensory disturbance has subsided, electricity and massage should be resorted to; and in those patients whose ill-health is traced to sleeping in a bedroom the wall-paper of which contains arsenic, the individual should be at once removed from that room, sent away for change of air to another locality, and meanwhile the walls of the room stripped of the paper.

PHOSPHORUS POISONING.

Etiology.—Poisoning by phosphorus is acute or chronic. In the acute form the symptoms are consequent upon swallowing the non-metallic substance known as phosphorus, usually with suicidal intent. The symptoms of chronic poisoning are mostly observed among match-makers. In England phosphorus poisoning is mostly suicidal. During five years ending 1890, thirty-six fatal cases of phosphorus poisoning occurred, fourteen males and twenty-two females; during the quinquennium ending 1895 there were sixty-seven fatal cases. Poisoning by phosphorus is a painful and not always a rapid method of self-destruction, and yet, in spite of this fact, which is pretty generally known, men and women, but particularly women, either through jealousy, drink, ill-usage by their husbands, or through poverty, heedlessly resort to drinking a solution of match heads in water as a means of terminating their life. The common vermin pastes, since they contain phosphorus in a finely divided form, are also resorted to for this purpose. Of the two varieties met with in commerce, it is the yellow or white, as distinguished from the red or amorphous phosphorus, that is so poisonous. Obtained from the bones of animals by operating upon them with sulphuric acid, and subsequently reducing the resulting superphosphate by means of charcoal in retorts, at a high temperature, phosphorus exists as a soft, solid, waxy, transparent substance, which emits a strong garlicky odour, is rapidly oxidised, and is so inflammable that it must be kept under water. Yellow phosphorus is in this country mostly used in the manufacture of ordinary matches. The red or amorphous form not only does not catch fire at the ordinary temperature like the yellow, but is practically non-poisonous, and is used for making "safety" matches. This form, which was invented by Schrötter, is obtained by heating the common phosphorus in closed iron vessels to a very high temperature, whereby it is rendered colourless, loses its phosphorescence, does not strike on percussion or moderate friction, and as stated is non-poisonous.

It is a little more than half a century since the profession became familiar with phosphorus poisoning. There is an opinion that the sulphur match tipped with phosphorus originated in Stockton-on-Tees, but as Vienna became the centre of the friction match industry, it is to Austria and certain parts of Germany that we look for the early reports of poisoning. Although matches began to be made in 1833, it was not until 1845 that Lorinser reported twenty-two cases of poisoning; from that date onwards until now, facts have been accumulating which point to phosphorus as a substance extremely inimical to life, and its fumes as capable of producing in people who are exposed to them serious disease of the bones of the jaw.

In nearly all the departments of a lucifer match factory there are unpleasant fumes evolved, but some departments are much more dangerous to health than others. The "composition" used for match heads consists of phosphorus, potassium chlorate, glue, antimony sulphide, manganese peroxide, powdered glass, and colouring matter. It is not necessary that the paste should contain more than 5 per cent. of phosphorus. It is to the presence of potassium chlorate in the match head that when struck the rapid ignition and the sharp explosion are due. The person who stirs the "composition," the people who dip the matches into it, and those who are engaged in the boxing-room, inhale more or less of the obnoxious fumes; hence these de-

partments are all more or less dangerous. In the manufacture of " safety " matches, and many of those that come from Sweden, there is less risk to health, owing to the red or amorphous and not the yellow phosphorus being used; whereas in France, particularly in Marseilles, so distinctly recognisable were the effects of the fumes upon the health and constitution of the match-makers, that the term *phosphorism* was employed to designate the intoxication that is slowly developed, and in which cachexia, a garlicky odour of the breath and saliva, anæmia, abortion amongst women, a high rate of infant mortality, albuminuria and cystitis are the most prominent symptoms.

Morbid anatomy and pathology.—Numerous small hæmorrhages may be observed in the skin, on the mucous and serous membranes, and between the muscles. The cadaver is generally bile-stained, and there arises from it a strong odour of phosphorus. The liver is enlarged and fatty, but it may be shrunken, from disintegration of the hepatic cells, if the patient lived for some time after taking the poison. The spleen may or may not be enlarged. Nearly all the internal organs will be found to have undergone fatty degeneration, a condition which involves even the small blood vessels. This widespread fatty degeneration is believed by Bauer and others to depend upon chemical changes in the cellular protoplasm, consequent upon inefficient oxidation, for during life less oxygen is found to be absorbed than in health and less carbonic acid formed. The hæmorrhages in the skin may be consequent upon fatty changes in the blood vessels, or they may come, as Thoma asserts, from capillaries, whose walls, whilst exhibiting no striking pathological changes, are yet more permeable, especially the intima, which under normal conditions only allows the fluid part of the blood to pass into the tissues, but restrains the cellular elements. To the destruction of hepatic and red blood cells, to imperfectly formed biliary salts, and the resulting catarrhal condition of the lining membrane of the small biliary ducts consequent upon irritation by the unhealthy bile, leading thereby to obstruction followed by absorption, must be attributed the jaundice in phosphorus poisoning. In consequence of the fatty degeneration of the liver and kidneys, the functional activity of these organs is so impaired that they allow of the retention of animal poisons within the system, and as a result of this, and the excess of lactic acid circulating in the blood, there develop somnolence and coma.

Phosphorus is known to exercise a stimulating influence upon the nutrition of bone. In chickens that had received phosphorus in their food, the bones were found to be extremely hard; all spongy tissue had disappeared, and was replaced by dense bone, in which the Haversian canals were obliterated. Kassowitz repeating these experiments of Wegner, found that such was the fact up to a certain point only, for if he pushed the administration of the phosphorus the medullary spaces became larger, and the bones presented the appearances found in rickets. It is upon work-people exposed to its malevolent fumes that the injurious effects of phosphorus are principally seen, and for a knowledge of which we are largely indebted to Wegner. Match-makers hardly ever exhibit the symptoms of acute poisoning, while, on the other hand, people who have taken internally large doses of phosphorus do not suffer from the painful affection of the jawbone. To this general statement there are exceptions, as for example the case of a girl reported by Fournier and Ollivier, who, in addition to necrosis of the jaw, exhibited symptoms of

acute poisoning along with purpuric hæmorrhages, and cerebral symptoms ending fatally in six days, and in whose internal organs no fatty degeneration was detected. Wegner found that the experimental administration of the poison was not followed by periosteal changes, unless he bared the tibiæ and exposed the animals to the fumes of phosphorus, when periostitis followed. It is in the inferior maxillary bone of lucifer match-makers that the ravages of phosphorus are principally seen, in the form of periostitis, leading to necrosis. There is first toothache, which is not relieved by extraction of the tooth, nor followed by an early closing of the wound, for it continues to discharge a foul, offensive pus, the gums keep ulcerating, and through the opening are discharged pieces of dead bone. The disease may limit itself or require to be dealt with surgically, but in some patients the morbid process advances, until nearly the whole of the jawbone is involved, when the constitution becomes undermined through the progressing necrosis and septic absorption, emaciation and hectic become well marked, and death comes not seldom through tuberculous disease. Among the makers of the phosphorus vermin pellets, which are sold in Saxony, Zehnter found bronchitis and broncho-pneumonia not uncommon symptoms.

Industrial phosphorus poisoning.—In match factories where white phosphorus is used, it is the mixing, dipping, and boxing departments that are the most dangerous. Both the mixer and the dipper run the risk of inhaling the phosphorus fumes. These fumes are composed of phosphoric oxide (P_4O_{10}), phosphorus oxide (P_4O_6), and phosphorus. The girls who fill the boxes have to handle the matches, and as these frequently become ignited, dense clouds of an irritating smoke arise, which cannot but be inhaled. It is no uncommon thing to see the hands of the girls stained from contact with the match heads; they smell strongly of phosphorus, and if not washed they are luminous in the dark. Thorpe found as much as 37 mgrms. of phosphorus in the water in which the workpeople had washed their hands. The poison may thus gain an entrance into the system, through workpeople eating with unwashed hands, or through inhaling the fumes of phosphorus pentoxide (P_4O_{10}) during combustion of the matches. But there is another channel of entrance to which we shall allude. It is strange that match-makers should suffer from phosphorism and from phosphorus necrosis, while the makers of the white or yellow phosphorus very largely escape. Most of the phosphorus used in Europe is made either at Oldbury, near Birmingham, or at Lyons, and it will give the reader some idea of the magnitude of the match industry, when I mention. that upwards of 1200 tons of white phosphorus are used annually in the manufacture of lucifers. Of this amount 60 tons are consumed in the match works of Great Britain and Ireland. There has been considerable discussion, both in the British and foreign parliaments, owing to the amount of illness among match-makers, as to whether the use of white phosphorus should not be entirely prohibited. In the United Kingdom there are twenty-four match factories using the yellow phosphorus, and giving employment to 4500 people, of whom 1908 are engaged in the dangerous processes. From 1893 until the end of June 1898 there have been notified to the Home Office thirty-one cases of phosphorus necrosis, and during 1897 this caused two deaths. Two years ago the French Government appointed a commission to inquire into the subject of phosphorism among the match-makers of Pantin-Aubervilliers. Out of 620 men and women employed in these works, 124 were found to have

painful carious teeth, and of these people twenty had suffered from necrosis of the jaw between 1890 and 1897. At Grammont, one of the principal seats of match-making in Belgium, and which contains six factories giving employment to 1100 people, Brocorens, between 1860 and 1895, met with thirty-four cases of phosphorus necrosis with eleven deaths. Kocher, in 1894, estimated the proportion of cases of necrosis in Switzerland to be equal to two to three per cent. of the workers. Kuiypers has reported eighteen cases of phosphorus necrosis treated in Jena Hospital, 1890–95. The principal accident which befalls a match-maker is necrosis of the jawbone. It is believed that through a penetrating caries of the teeth the phosphorus fumes find their way into the deeper structures, setting up a septic periostitis, followed by necrosis of bone. It is more than likely that other agencies are at work in addition to the fumes. In the discharges from the necrotic jaws of match-makers I have found such putrefactive micro-organisms as staphylococci and streptococci, while Stockman found tubercle bacilli, and consequently he considers phosphorus necrosis to be very largely a tuberculous disease of the bone. During twenty-five years Brocorens met with thirty cases of spontaneous fracture of bone caused by muscular effort, and affecting exclusively the lower extremities, in workmen who had been employed as "dippers." More than one-half of these men had previously suffered from necrosis. The fractures healed as readily as in other people.

In addition to necrosis and fracture of bone, there is another form of phosphorus poisoning induced, namely, phosphorism characterised by cachexia, a peculiar yellow tinge of the skin and albuminuria. Good teeth in match-makers are regarded as a protective. No person with carious teeth ought to work in the dangerous departments of a match factory. It is not always easy to detect the early stages of phosphorus intoxication. Albert Robin claims that he has found out a diagnostic sign of great importance. Normally the amount of mineral substances in the urine is one-third of the whole of the solids (30 in 100). In phosphorus-poisoned people he found the ratio frequently as high as 50 or even 60 per cent. The "co-efficient of demineralisation" is, according to Robin, in match-makers almost double of that in health. It is to the increased "co-efficient of demineralisation" that Robin attributes the tendency to necrosis and the fragility of the bones of match-makers. Arnaud, who has had a very large experience of industrial phosphorism, did not find this elevated coefficient; in match-makers he found the average to be 33·85.

It has been my fortune to visit officially for the British Government match works in Britain, France, Belgium, and Prussia. I can bear testimony to the extreme painfulness of phosphor necrosis, particularly in the early stages. Extraction of the teeth gives no relief. The half of the face in time becomes swollen, and the tissues about the jaw infiltrated. On examining the mouth, the alveolar surface of the bone is observed to be exposed and covered with a thick yellowish slough, from which only a small quantity of pus escapes. The glands underneath the jaw are frequently enlarged, and occasionally there is a fistulous opening under or on the cheek. Necrosis may affect either jawbone, more frequently the inferior maxilla. If the disease is limited to the lower jaw, and is surgically treated, either by gouging out a piece of bone or resecting it, the patient is generally able to return to work in about fourteen months; but when necrosis invades the superior maxilla, there is a greater tendency for the disease to spread

upwards and backwards, and to induce some brain affection, either a septic meningitis or a cerebral abscess, and which is fatal.

Symptoms.—In acute phosphorus poisoning the symptoms usually appear within from one to six hours, but their severity and the period at which they appear depend upon the finely divided form in which the phosphorus is taken, its quantity, and the absence or presence of fatty or oily food in the stomach at the time. If milk or fatty food is present, it dissolves the poison, hastens its absorption, and causes an early appearance of the symptoms. Less than 2 grs. of phosphorus have proved fatal. Match heads contain phosphorus varying in amount from 3·5 to 7·5 mgrms. (·058 to ·116 gr.), so that the solution of twenty to a hundred match heads might, if drunk, cause death.

For a few hours after taking phosphorus the individual may move about, and his behaviour be such as not to attract attention, but gradually abdominal pain supervenes, followed by nausea and vomiting, and then the individual, on account of pain, is forced to tell the story of his attempted suicide. During the act of swallowing, a disagreeable taste is experienced in the mouth, succeeded by a burning sensation in the gullet and stomach, and subsequently by retching and vomiting. The breath and vomited matter reek of the odour of phosphorus. The vomit contains blood or biliary colouring matter, and may be luminous in the dark. Coffee-ground vomiting may continue for two or three days, and be accompanied by diarrhœa. At this stage the majority of patients become jaundiced, and the rapidity with which this coloration of the skin appears may be taken as a measure of the severity of the poisoning. Contemporaneously with the appearance of jaundice, the liver on percussion and palpation is observed to be uniformly enlarged and somewhat tender, but subsequently it commences to shrink, a circumstance which, with deepening of the jaundice, suggests the probability, in the absence of a history of phosphorus poisoning, of the case being one of acute yellow atrophy of the liver. The pulse is weak and rapid, frequently reaching 150 per minute; the temperature varies. A high temperature is usually regarded as an omen of death, but I have met with a fatal case where the thermometer at this stage registered only 96° F. The urine may be albuminous; it is bile-stained, and frequently contains crystals of leucine and tyrosine. In some cases the symptoms subside, and the improvement is permanent; in others, the improvement is only temporary. Delirium with convulsions or coma supervenes, indicating, along with deepening of the jaundice, that the patient is no longer suffering from the simple effect of the poison, but that profound structural changes have been established in the liver and other internal organs. In children the illness may terminate fatally within the first day, before jaundice has had time to develop; one of the earliest cases on record being reported in a child æt. 8 months, who died within two hours of its mother pushing six matches down his œsophagus. On the average, death supervenes about the seventh day.

The acute form of poisoning just described corresponds to the common variety of Tardieu, in which the symptoms are irritant, nervous, and hæmorrhagic. Nervous symptoms occasionally predominate, there being, in addition to the vomiting and abdominal pain, cramp-like feelings in the legs, with loss of power, or delirium with convulsions, but without jaundice. Usually the skin is the seat of well-marked icterus, erythema, or petechial hæmorrhages. The liver is enlarged. Von Jaksch found the

alkalinity of the blood diminished, and the coloured discs temporarily increased in size. Munzer also found the blood less alkaline than in health, and attributed the fact to an increased production of acids within the body. It seemed to him that both the red and white blood corpuscles were normal in size, but that the red were increased in number. There is considerable discrepancy among writers as to the effect of phosphorus upon the blood. Binz, quoting as his authority Dybkowsky, says that the red blood corpuscles of man undergo no change. Whatever may be the primary effect of phosphorus upon the blood, it is now generally admitted that secondarily the number of the coloured discs is diminished. The blood, too, is of a darker colour, and is not so liable to coagulate as in health.

The urine may be albuminous and bile-stained, but sugar as a rule is absent. Tyrosin, if present, must be regarded as an indication of the existence of structural changes in the liver, tending to fatty degeneration and atrophy. On microscopical examination of the kidney, the epithelium is found to be fatty, and hyaline tube casts, which are often bile-stained, may be observed *in situ*. Munzer found crystals of hæmatoidin in the urine, also traces of sarcolactic acid. A transitory peptonuria is alluded to by some authors, and a fall in the total nitrogen eliminated in the early stages is vouched for by von Jaksch, and corroborated by my own experience. Subsequently the nitrogenous waste in the urine, as indicated by uric acid and ammonia, may be increased, the ammonia playing, according to Munzer, a useful part in the economy, by neutralising the acid products formed in excess through the action of phosphorus upon the tissues. Phosphoric acid, if present in the urine in excess in the early stages, subsequently, along with the sulphuric acid, sinks below the normal. So long as jaundice is present, the fæces are pale: they may contain phosphorus, and emit a garlicky odour. Pregnant women usually miscarry, the fœtus as a rule being still-born. There is nothing unusual in the course of the labour in such a case, but once it is completed the jaundice is frequently observed to deepen in tint, the liver becomes more tender, and rapidly shrinks in size. Somnolence develops, and the patient dies comatose.

Diagnosis. — When the liver is shrunken and jaundice well marked, phosphorus poisoning resembles acute yellow atrophy of the liver. Delirium and coma are perhaps not just so pronounced in phosphorus poisoning, and there is less tendency for the spleen to be enlarged. It is noteworthy, too, that whilst in acute yellow atrophy the liver decreases rapidly in size, and the jaundice deepens in proportion, in phosphorus poisoning, on the other hand, the jaundice appears with the enlargement of the liver and runs parallel with it. The urine is more likely to contain leucine and tyrosine in acute yellow atrophy, the leucine appearing as small spheres, not unlike droplets of fat, and tyrosine as delicate needle-like crystals. At the autopsy it has sometimes been impossible to distinguish between the two diseases. There are physicians who maintain that, apart from phosphorus poisoning, there is no such independent disease as acute yellow atrophy of the liver. Vivian Poore holds that clinically and pathologically the two conditions are indistinguishable.

Hypertrophic cirrhosis of the liver may resemble subacute phosphorus poisoning, especially if it is rapidly developed and leads to death through cholæmia. No reliance can be placed upon the sanguineous vomit nor enlargement of the spleen, which is said by some to be present in hyper-

trophic cirrhosis as differentiating the disease from phosphorus poisoning, for after all these are not always present in hypertrophic cirrhosis. The recurrence of convulsions or rigors, a high temperature, albuminuria, splenic enlargement, and the history of the case, would help to distinguish puerperal eclampsia with jaundice, also certain forms of alcoholic and uræmic intoxication, and septic infection from phosphorus poisoning. The odour of phosphorus in the vomit and fæces would settle the diagnosis of acute poisoning.

Prognosis.—The prognosis of phosphorus poisoning is grave, the gravity being proportional to the dose taken. Nearly 40 per cent. of the patients die, some within two or three days after taking the poison, others several days afterwards and rather suddenly, from syncope due to fatty degeneration of·the cardiac muscle fibre; while others, again, die in a state of delirium and coma, the early appearance of which, along with the jaundice, must be regarded as a measure of the severity of the illness.

Treatment.—If seen early, emetics and purgatives should be at once administered, in the hope of preventing absorption, for once this has taken place it is impossible to control the organic changes that follow. To be efficacious, treatment should be resorted to at once, and be continued. Washing out the stomach with an abundant supply of lukewarm water is at once called for, until all odour of phosphorus has disappeared, and adding to the final lavage copper sulphate (1 in 100), since this forms, with any phosphorus left in the stomach, an insoluble phosphide of copper. Von Jaksch recommends irrigation of the stomach with water containing gelatin and magnesia, others use potassium permanganate, whilst Andant and Personne speak highly of the essence of terebinthin in capsules, 1 to 2 drms. in twenty-four hours. In this country the administration of oil of turpentine in 40-drop doses, though not so beneficial as the old French oleum terebinth, gives, on the whole, satisfactory results. This is due to the fact that phosphorus, having a great affinity for oxygen, combines with the nascent oxygen in the turpentine, forming a harmless compound, probably phosphoric acid. All fatty food, such as milk, and oily emulsions, which rapidly dissolve phosphorus, must be interdicted. Saline aperients are necessary, even after the use of emetics and the stomach-pump, but castor-oil must be avoided.

In the later stages, when the heart has undergone degeneration and there is faintness, stimulants should be administered with or without the hypodermic injection of digitalin, ether, etc.

The treatment of phosphorism, as observed among match-makers, is preventive and curative. Ill health would practically disappear, if red phosphorus were substituted for yellow in the manufacture of matches. In Denmark the use of yellow phosphorus in match-making is interdicted. Other nations are moving in a similar direction, and are either insisting upon matches being made in closed machines, or of replacing the white by the harmless red phosphorus. Kassner, a Frenchman, has invented matches made of plumbate of calcium, which, while retaining all the advantages, have none of the disadvantages observed in those made from phosphorus. In France matches are now made from the harmless sesqui-sulphide of phosphorus. Enfeebled, poverty-stricken, and intemperate people should not be allowed to enter upon or continue at the trade. The workshops should be well ventilated. Personal cleanliness should be insisted upon, and there should be frequent dental examination of the teeth and gums, so that, in the event of carious teeth being detected in an individual, he

should be obliged to retire from the factory. For the early stages of phosphorus necrosis or "phossy jaw," as it is sometimes called in this country, "*mal chimique*," as it is known in France, antiseptic mouth-washes are necessary. Magitot and Roussel believe that caries of the teeth precedes the necrosis, and that this allows of the penetration of the phosphorus fumes, whereby periostitis is induced; but Dubois states that he has never observed any primary dental lesion or any affection of the gums in match-makers. Riedel maintains that in phosphorism, periostitis ossificans of the jawbone may occur before there is necrosis, if the teeth are good. Once necrosis is established, medicine does no good. Early surgical intervention is advised by the German surgeons, Riedel, Langenbeck, Pitha, and Billroth, who are in favour of complete resection of the jaw; but English and French surgeons prefer to wait until the sequestrum is removable. Among the lucifer match-makers of the East End of London, Garman found that he got less deformity of the face when the sequestrum was allowed to come away of its own accord, and that the rate of mortality was lower than when the cases were treated surgically.

MERCURIAL POISONING.

Etiology.—Poisoning by mercury may be acute or chronic. The chronic form hydrargyria, or mercurialism, is observed among the miners and smelters of quicksilver, in people who handle the metal or inhale its vapour during the manufacture of mirrors, barometers, and thermometers, also among felt hat makers and furriers. Some persons have a greater susceptibility to the poison than others. Women and young children are, if anything, more liable to be affected by it, also people suffering from kidney disease, and those who are scrofulous. Rigler states that opium-eaters can take fairly large doses of corrosive sublimate with greater impunity. The metal gains access to the system by absorption through the skin, by inhalation of the vapour, and by workmen eating with unwashed hands.

Acute mercurial poisoning is chiefly suicidal, and in this country is responsible for about five deaths every year. During ten years ending 1892, fifty-nine deaths occurred in England from mercury, mostly from corrosive sublimate, namely, forty males and nineteen females; and of these there were sixteen males and eighteen females whose poisoning was suicidal. The toxic effects of all the mercurial compounds are similar, but as corrosive sublimate produces the most violent symptoms, it is generally taken as the type of this form of poisoning.

Mercury comes into this country in the form of sulphide or cinnabar, from which, either by roasting the ore or reducing it with iron and lime, metallic vapour is given off, which readily condenses. Until lately, most of the mercury came from Almaden in Spain, but California as a producer has lately rivalled Spain. It has been known for centuries that the fumes of the metal have at Almaden played havoc with the workpeople and vegetation. As it was difficult to get men to work in the mines or at the smelting furnaces, gangs of convicts had to be imported, but as their habits were even less cleanly than those of the ordinary workmen, they readily fell victims to the unhealthy air of the mines, or the heavily laden

atmosphere of the smelting rooms. The application of better sanitary laws, and the introduction of improved methods of mining and smelting, which the wealth of California allows of, have in the United States largely contributed to the obviation of many of those objectionable conditions to the operation of which much of the ill-health of the Spanish miners was attributed.

It is owing to its ready volatilisation that mercury is such a dangerous metal in the industries. Workmen exposed to its vapour at a low temperature scarcely suffer, but mercury begins to volatilise at 8°·5 F., and the danger increases with elevation of the temperature. It readily forms an amalgam ·with other metals, from which it can be easily separated by distillation. Thus, united with gold or silver, it was used by water-gilders for depositing gold on metallic surfaces, also in mirror-silvering, processes which were · attended by a considerable amount of ill-health on the part of those thus employed. Water-gilding has lately been superseded by electro-plating, and the silvering of mirrors is now accomplished by pouring a mixture of tartaric acid and silver nitrate on glass, and exposing it to the air, when the silver becomes deposited. In my visits to the largest glass-works of this country, I have observed that since the adoption of the new method of silvering mirrors, workmen no longer suffer; but in going through boot and shoe factories, where American sole-stitching machines are employed, my attention has been drawn to supposed symptoms of mercurialism among men who work these machines, owing to mercurial vapour arising from a well or movable joint which is filled with quicksilver.

Poisoning is also observed among hatters in Germany and America. Felt is made from the furs of various animals, *e.g.* the beaver, rabbit, and hare; whilst coarser kinds are made from wool and cotton. Furs blend and adhere better after felting, if they have been treated with a strong solution of acid nitrate of mercury. This is accomplished by brushing the fur with the mercury, a process which at this stage is not dangerous. The danger arises subsequently when the felt is being made into hats or is being finished, for at this stage a considerable amount of dust is given off; it is likewise present when the finished material is subjected to great heat, for then mercurial vapours escape. As a class, hat makers show a higher mortality than most of the other trades, their death-rate in England being 1064 to 1000 of all males.

Among other causes of accidental, suicidal, or homicidal mercurial poisoning from corrosive sublimate, may be mentioned the external application of nitrate of mercury, the absorption through the skin of certain salts, *e.g.* the oleate, also the employment by surgeons and accoucheurs of too strong solutions of the perchloride as a germicide in washing out the internal cavities of the body.

Morbid anatomy.—If a person has died from corrosive sublimate poisoning, there is escharotic whitening of the mouth, throat, and gullet; there is considerable destruction of the mucous membrane, or it is ecchymosed all the way down the intestinal tract to the anus. Irrespective of the channel by which mercury has gained entrance into the system, the intestine usually contains a large quantity of yellowish brown or sanguinolent liquid, accompanied by flakes of mucous membrane. The kidneys are hyperæmic, and the renal tubules contain chalky masses, consequent upon decalcification of the bones, and a subsequent deposition of lime salts in the kidneys. In animals experimentally poisoned by the injection of peptonate of mercury, death supervened too rapidly from

paralysis of the heart for pathological changes to be observed; but in cases where life for a time was maintained, the myelin sheath of the peripheral nerves was found fatty, and in the spinal cord there was observed a limited myelitis. In mercurial encephalopathy there have been found cerebral œdema, fluid in the subarachnoid and ventricular spaces with arterio-sclerosis, and, on chemical analysis, mercury has been found in the brain.

Symptoms.—In people who have been exposed to the vapour of mercury, tremor is frequently observed. Commencing usually in the upper extremities, it spreads to voluntary muscles, and in doing so increases in amplitude, ultimately assuming a choreiform character. The movements are aggravated by emotion, and generally cease during sleep. There may be paralysis, and if so, the tremor may be entirely confined to the muscles thus affected. Although their electrical reaction is diminished, the muscles do not exhibit any qualitative changes to the galvanic current. Want of personal cleanliness, ill-feeding, and the abuse of alcoholic stimulants, on the part of the work-people, predispose to tremor. The gums become swollen, ulcerated, and tend to bleed, the teeth become loose and fall out. The salivary glands are excited to unwonted activity, either reflexly by irritation of the tongue, which feels too large for the mouth, by stimulation of the nerves that supply the glands, or by changes in the glands themselves, for these are enlarged and painful. The breath is fœtid, and there is complaint of a disagreeable taste in the mouth. The changes in the gums occur without pain or fever. The miners at Almaden used to regard the loss of their teeth as likely to give them exemption from further trouble, but the shedding of the teeth destroyed their power of mastication, and so altered their facial expression that while they were still young they looked like old men. Add to tremor and loss of teeth, the presence of anæmia or cachexia, bronzing of the skin, a rash known as "eczema mercuriale," diarrhœa, rheumatic pains in the joints, and fœtid breath, symptoms which are spoken of as those of mercurial scurvy; also a tendency for pregnant females to abort, and the children born of affected parents dying largely from phthisis, and we have a symptomatology which is characteristic of chronic mercurialism.

Occasionally, the paralysis is limited to one or a few muscles, and is accompanied by an alteration of speech, which becomes staccato and stammering. The loss of power is preceded by pain, suggesting peripheral neuritis, or there is surface anæsthesia, which suggests hysteria. There may be other symptoms too, such as are observed in hysteria, namely, hemiplegia, hemianæsthesia, and amblyopia. Several of these cases have in the hands of Letulle rapidly yielded to suggestion, clearly indicating that there could not have been in the nervous system any organic lesion. A low form of encephalopathy is occasionally developed in mercurialism, in which the intellectual powers become blunted, the mental faculties lose their sharpness, and sleeplessness supervenes, followed by insanity. The special senses do not always escape. There may be amblyopia, or optic atrophy.

After swallowing a large dose of corrosive sublimate, severe symptoms appear usually within half an hour. The bichloride is a powerful poison. Three grains have proved fatal. The patient complains of a burning heat in the throat, with a sense of constriction during the act of swallowing the poison. There is pallor of the mucous membranes with shrivelling, great pain in the stomach, profuse diarrhœa, and bloody vomiting; marked

fall of the temperature, small and irregular pulse, scanty urine, extreme prostration and collapse, œdema of the glottis, followed by difficult breathing and asphyxia, leading to death, which may be preceded by convulsions or be due to syncope. Some people are extremely easily influenced by mercury. As illustrating this susceptibility, I will mention one case, that of a girl, aged 18 years, who was suffering from anæmia. I ordered her 2 grs. of calomel. After a second dose of 2 grs., taken several days after the first, the patient was severely mercurialised. She had headache, inflamed eyes, salivation, and painful ulceration of the gums.

Diagnosis.—The history of the case, and particularly if the poisoning is acute, the presence of white eschars in the mouth, extreme pain at the epigastrium, sanguinolent vomiting, and diarrhœa with collapse, suggest the probability that corrosive sublimate has been taken. The tremor observed in a chronic case is not unlike that of disseminated sclerosis, but there is neither the nystagmus nor the exaggerated reflexes noticed in that disease, whilst the tremor, similarly exaggerated under volition, is much less in amplitude. Speech in both illnesses may be affected, but it is more a stuttering in chronic mercurialism than the slow syllabic speech observed in disseminated sclerosis. Hydrargyria may simulate progressive general paralysis, but there are no grandiose ideas, although there is mental irritability; no inequality of the pupils; and although tremor is present in both, it is distributed all over the body in mercurialism, whereas it is confined to the lips, tongue, and hands, in general paralysis. It may be difficult to distinguish between chronic mercurialism and lead poisoning, if tremor is the only symptom; but in the history of colic, the presence of a blue line on the gums, and in the results of an examination of the urine for lead or mercury, an answer to the problem will be found.

Prognosis.—In acute poisoning by corrosive sublimate, the prognosis depends upon the dose swallowed and the severity of the symptoms. It is grave as a rule. In chronic mercurialism, unless the individual has been too long exposed to the fumes of the metal, he generally does well, if removed from the cause of his illness. In chronic cases, life is only threatened when the kidneys have become profoundly affected, or where the brain is the seat of mercurial deposition. Tremor once established may never entirely disappear, but its persistence need cause no anxiety.

Treatment.—The treatment of chronic mercurialism is preventive and curative, whilst that for corrosive sublimate is largely the employment of the ordinary remedies useful in acute irritant poisoning. In the case of work-people exposed to the fumes of the metal, it may be impossible to prevent some degree of poisoning; but good ventilation, personal cleanliness, washing of the hands before eating, the frequent use of baths, working in cool rooms to prevent perspiration, no food to be eaten in the workrooms, and change of occupation on symptoms showing themselves, are regulations which, when followed, will largely diminish industrial mercurialism. Mouth washes composed of weak carbolic or boracic acid, or of potassium chlorate, myrrh and quassia, are advantageous where the gums are soft and ulcerating. Iodide of potassium has the reputation of favouring the elimination of mercury, but it should be given carefully, commencing with small doses, so as not to throw at one time too much of the metal redissolved from the tissues into the circulation. Milk diet favours elimination by the kidneys. Sulphur baths are recommended, but they are doubtfully efficacious, and for the paralysis and muscular weakness, electricity and massage, employing the galvanic current in

the early stages, and subsequently, when the muscles are atrophied, faradism.

In acute poisoning, treatment may be unavailing, but advantage is taken of the fact that mercury forms with albuminous bodies insoluble compounds, to administer milk and white of egg. The stomach must be thoroughly washed out, and vomiting encouraged, either by subcutaneous injection of 4 drop doses of apomorphine, or by zinc sulphate given by the mouth. For severe pain morphia must be administered, and for collapse stimulants or caffeine by the rectum. Occasionally the symptoms subside, and while the patient is apparently progressing there is a return of the dysenteric discharges, accompanied by ptyalism and great debility, to which the patient may succumb. If decalcification of bones is taking place, lime salts should be given, *e.g.* calcium phosphate.

In obstetrical practice, too free irrigation of the uterine cavity, with even weak solutions of bichloride of mercury, has caused symptoms of poisoning. It is noteworthy that nearly one-half of those who have suffered were primiparæ. Bichloride of mercury should not be used where the mother is anæmic or debilitated, as a consequence of her pregnancy or from hæmorrhages; and the accoucheur should be quite sure of the integrity of the kidneys, as experience has shown how susceptible renal patients are to the influence of mercury.

ALCOHOLIC POISONING.

Etiology.—There is no product of human ingenuity more widely distributed throughout the world than alcohol. Almost every nation has its alcoholic beverage, or its stimulant and narcotic. It is to the effects caused by the immoderate use of alcohol that we intend particularly to refer. The word itself shows how conscious the Arabs of old were of its effects when they named it alcohol—*al* the, and *Kohol* secret, or subtle thing—the use of which robbed the individual of his senses. All the alcohols are poisons. The four most important, and they are given in the order of increasing toxicity, are — (1) methylic alcohol, a wood spirit; (2) ethylic alcohol, or spirit of wine; (3) propylic; and (4) amylic alcohol, fusel oil, or potato spirit. Spirit of wine, usually spoken of as alcohol, the prefix ethylic being omitted, is obtained from the alcoholic fermentation of sugar. It always contains water, part of which only is removable by redistillation, for the strongest rectified spirit usually contains from 13 to 16 per cent. of water. A further portion of the water can be removed by distillation with quicklime. When thus purified, it is called *absolute alcohol*, and contains 1 per cent. of water. Methylic alcohol, or wood naphtha, is obtained from the dry distillation of wood; while methylated spirit is a mixture of nine parts of ethylic alcohol (spirits of wine) and one part methylic. The percentage of alcohol in spirituous beverages varies: whisky, brandy, and gin contain from 50 to 60 per cent.; port and sherry, 15 to 20; claret and burgundy, 10 to 17; champagne, 6 to 13; ale and porter, 4 to 6 per cent. Alcohol is a colourless limpid fluid, with a pungent taste and agreeable smell; it has a strong attraction for water, whether in the air or in the tissues of an animal, and is easily converted by oxidation into aldehyde and water, and subsequently into acetic acid.

Morbid anatomy and pathology.—Alcohol is a narcotic poison, which exercises its pernicious influence principally upon the brain, as witness simple intoxication, in which the various centres in the brain at particular levels become successively involved. After death from coma, in acute alcoholic poisoning, the brain and its membranes are found injected, and there is inflammatory redness of the mucous membrane of the stomach and duodenum. In the bodies of chronic drinkers, degenerative changes are found widely distributed. The liver is fatty or cirrhotic; the spleen is enlarged and contains excess of connective tissue; the gastric mucous membrane is congested; the heart is dilated and its muscle fibres soft and flabby; the aorta is atheromatous and dilated. Sometimes the membranes of the brain are thickened and adherent at the vertex; the pia mater is opaque. This pachymeningitis causes flattening of the cerebral convolutions, the blood vessels dipping into which are often found to be tortuous and degenerated. On microscopical examination, the large cells in the cortex of the motor areas show degenerative changes, along with vacuolation of their protoplasm, whilst their dendritic processes are varicose, and the surrounding neuroglia is increased. Similar changes may be observed in the spinal cord, affecting principally the ganglion cells. In the peripheral nerves of alcoholic paralytics there is frequently found excessive growth of the connective tissue framework, leading to atrophy of the nerve fibrils. It is an interesting fact as bearing upon the relation of alcoholic insanity and a predisposed state of the nervous system, probably hereditarily acquired, that in the experience of asylum pathologists, cirrhosis of the liver, which in infirmary practice is one of the most common effects of alcoholic intemperance, is almost never met with. This circumstance indicates that long before the effects of alcohol have had time to induce pathological changes in the liver, the nervous system, being unstable, has already become affected.

Symptoms.—The most common form of acute alcoholism is intoxication. This in its milder varieties involves the motor apparatus, and the organs of the ordinary and special senses. It is associated with varying mental phenomena, and when pushed further causes coma, or such a degree of excitement of the brain as to lead to insanity. One of the earliest effects of the imbibition of alcohol is relaxation of the blood vessels; this is accompanied by a sense of warmth and a general feeling of pleasure. The brain for the moment works faster, so that ideation is increased, but even at this stage the individual has, owing to vasomotor paralysis, lost to some extent his control. There is emotional excitement, and for the time being the individual is another *ego*. The man who is ordinarily quiet, retiring, and inoffensive, becomes, under the influence of drink, obtrusive, talkative, and querulous; his articulation becomes indistinct, his words are apt to be slurred and interrupted, and should he be sitting and attempt to rise, he staggers, owing to muscular inco-ordination. In the more advanced stages of drunkenness the intellectual powers as well as the motor may be so depressed, that the individual lies in a helpless and unconscious condition, his life being solely dependent upon the activity of his respiratory and cardiac centres. Hughlings Jackson, in his application of Herbert Spencer's theory of evolution to the nervous system, remarks that evolution is an ascending development in a particular order, and is a passage from the most to the least organised, *i.e.* to say from the lowest, well organised centres to the highest, least organised centres, or, in other words, a progress from centres which are comparatively well organised at birth to those highest centres

which are continually organising through life. It is a passage from the most automatic to the most voluntary. The reverse of this is dissolution, a process which consists in "taking to pieces," in the order from the most voluntary to the simplest and most automatic. In dissolution the centres are not all evenly affected, and the action of alcohol exemplifies this. The highest centres, because they are the least organised, give out first and most; the middle centres, being more organised, resist longer; while the lowest centres, being most organised, resist the longest. Hence are explained, as the results of alcoholic intoxication—(a) the disorder of the intellectual and emotional faculties; (b) loss of co-ordination; and (c) the coma of an individual who is dead drunk, and in whom life is but the expression of the automatic activities of cardiac and respiratory centres. Did these lowest centres, which are well organised, not resist the longest, death by large doses of alcohol would be frequent. As the cardiac centre during embryological development is laid down in the fœtus before the respiratory, it is therefore the more highly organised, and it remains active to the last in alcoholic poisoning, constituting the *ultimum moriens.*

Where a large quantity of strong spirit has been drunk in a short space of time, or is taken by people exhausted by fatigue or chilled by cold, coma is quickly developed, the face becomes pale, the pupils dilate, the temperature rapidly falls below the normal, the pulse becomes thready, and the breathing stertorous. Death may follow within a few hours. One cold New Year's Eve I remember being called to see a man who had swallowed within the space of a few minutes a large bottleful of whisky; he had quickly become unconscious, and was dead in less than three hours.

Exerting, as alcohol does, its pernicious influence upon the brain and nervous system, it produces a variety of mental disorders of an insane nature, of which seven different forms may be recognised :—(1) There is temporary mental derangement, or simple intoxication, induced in anyone by the absorption of alcohol. (2) *Mania a potu,* in which the individual thus affected differs from the man who is simply intoxicated, in so far as he is the subject of violent mania. He cannot control his acts. In this state he is more or less forgetful of the circumstances that have occurred, and is apt to be violent and destructive without necessarily being in a passion. For the time being the individual is so "possessed," that he is driven to the commission of acts, it may be of homicidal violence, that are quite beyond his control, and subsequently beyond his memory. In a few minutes his outburst of maniacal excitement may be over, or it may continue for hours, being occasionally broken by periods of quiescence, during which the pulse which was strong and full, resumes its normal character—the temperature throughout never having risen. Since many people who are in the habit of getting drunk never pass into this maniacal state, and since it occurs regularly in those of a peculiar nervous temperament, even after taking what to others would be a very moderate dose of alcohol, *mania a potu* would seem to depend rather upon a peculiar diathesis, or some congenital instability of the nervous system, whereby it becomes easily excited and unduly responsive to small quantities of alcohol, than upon any excess of drink taken. A morbid nervous substratum, hereditarily acquired, underlies this condition, for the individual is predisposed to epilepsy or to some other form of nervous disorder. (3) In the third form, or *delirium tremens,* the individual is insane, and is the subject of delusions and illusions. He may not have been drinking immediately before his outburst of delirium. The attack is therefore not traceable to a particular draught of alcohol,

although it may arise after a single debauch. It occurs in people who are specially predisposed, and who are habitually taking spirituous liquors to excess. What that peculiarity of bodily or nervous constitution is that predisposes to it, it is difficult to say. Some have maintained that sudden abstinence is a cause, but while there is no proof of this, there is sufficient evidence that physical and mental conditions which lower the vitality of the nervous system, such as shock from injury or surgical operation, exposure to cold and overwork, precipitate an attack of delirium tremens. For several days before the outburst, friends may have noticed that the patient was not quite well, that he was off his food, fidgety, and sleepless, and, when seen by his medical attendant at this stage, there is a furred tongue, the skin is bedewed with a cold clammy perspiration, and the person looks jaded and is tremulous. In the midst of this, he passes, without further warning, into a condition of great excitement. In his delirium he may perpetrate acts of violence upon himself or others, in his attempts to escape from the ocular illusions and auditory hallucinations of which he is the unhappy victim. Flushed in the face and perspiring freely, with a rapid, full, but soft pulse, a thickly-coated tongue, and sleepless, he is with difficulty restrained. In his delirious moments he keeps muttering about business matters, or answers loudly to unreal voices; he may escape the vigilance of those who are nursing him, or he may overcome them by his superior force, and in his delirium leap from a window, or in a state of terror commit self-destruction. The fury may continue for two or three days, when it is succeeded by a state of great asthenia, in which the patient lies mumbling to himself, picking at the bed-clothes, occasionally returning answers to unheard questions, carrying on conversations or talking incoherently, but with a voice low and indicative of great prostration, the tongue brown and dry, the pulse small and rapid. Sleeplessness continues, and the organic functions are all more or less deranged. There may be retention of urine, requiring the use of the catheter, and the urine when drawn off may be albuminous. The delirium of the earlier stage is now replaced by one of great exhaustion, or it is paroxysmal; and although it is still violent, its spells are of shorter duration, and are accompanied by increasing prostration, which rapidly leads to death. (4) *Chronic alcoholism,* in which, while the individual is seldom or never quite drunk, he is, on the other hand, never perfectly sober. His nervous system, too long flushed with alcohol, breaks down, and the man becomes either imbecile or an epileptic. Convulsive seizures may alternate with paroxysms of mania, in which the individual, who is quite insane, may perpetrate deeds of criminal violence, of the nature of which he is perfectly unconscious, and in regard to which his memory is a complete blank. Occasionally seizures of an ordinary epileptic character occur without any maniacal phenomena. These are usually traceable to alcoholic indulgence, and are causally connected with it, for they disappear during total abstinence, and return with drinking. When an epileptic fit occurs for the first time in an individual who is addicted to alcohol, it is one of the earliest indications of the brain giving way, and is a symptom never to be disregarded, nor thought lightly of by the medical attendant. Underneath chronic alcoholism there is generally in operation an inherited predisposition to some form of nervous disease, which shows itself in a tendency to excessive drinking, suicide, epilepsy, or some other form of nervous disorder. (5) *Habitual drunkenness* constitutes the fifth variety. Although this is a condition practically speaking uncontrollable, it is yet within the conceivable control of the will. Gairdner, in his Class Lectures on

"Drink Madness," and whose classification I have adopted, thus speaks of habitual drunkenness as a condition in which "the moral nature is not yet completely sapped: the man is not utterly shameless in the indulgence of his desire: he may know and admit the folly of his course, but the power of the will is so weakened, and the taste so depraved, that in the work of life he is sure to go wrong." (6) *Dipsomania*, in which the individual is so much under the domination of appetite, that no consideration can control him, if by any possibility he can gratify it. During the weeks or months he is sober he knows that a time is coming when the craving for alcohol will be so great that, short of bodily constraint, nothing will prevent him drinking. In this and in the condition last described, the individual is unquestionably insane, and yet, because the mental phenomena depend upon a definite and recognisable material having been taken, namely, alcohol, the law is not disposed to recognise these as insanity. It holds that the man is just as responsible for his acts as if he were sober, although the same condition arising from unknown causes would certainly lead the individual to be regarded as insane, and therefore irresponsible. The law assumes that, as the individual voluntarily took that which made him insane, he is responsible for the mental condition which it has created, and it is the knowledge of this fact which obliges medical men to act with extreme caution in cases of drink madness, particularly delirium tremens, in which the civil rights and personal liberty of the individual cannot be interfered with, except at the greatest risk to those who thus seek to interpose. (7) *General paralysis, imbecility, and several neuroses,*—for these and other large questions bearing upon alcoholic insanity and legal responsibility, special text-books, however, must be consulted.

As a consequence of prolonged indulgence in alcohol, the central nervous system suffers, but the peripheral nerves do not always escape. Alcoholic neuritis is a well-defined clinical condition, dependent upon a recognisable pathological lesion. Men are more the subjects of delirium tremens than women, but women are more liable to alcoholic peripheral neuritis, an affection which attacks the legs oftener than the arms. Occasionally lethargy, disinclination for muscular exertion, and an increasing difficulty of walking, foretell the approach of the paralysis; while in other patients there are, as premonitory symptoms, burning pains in the soles of the feet, painful cramps in the calves, the muscles of which are extremely tender to the grasp, absent knee-jerks, and exaggerated cutaneous reflexes. Or there is patchy anæsthesia, flabby muscles, cold extremities and glistening skin, pain along the course of the nerves, and close upon these comes paralysis, *e.g.* double "ankle-drop" or "wrist-drop." Sometimes paralysis develops in the feet and legs simultaneously without any prodromata. The muscles rapidly waste, and cease to react to faradism. The urine may or may not contain albumin. In addition to organic changes in the nervous system, there may be observed in alcoholic patients certain morbid phenomena which are due to functional derangement of the nervous system, rather than to the existence of any altered structure, since they rapidly disappear under enforced abstinence, medicinal treatment, and rest. Alcoholic ataxia, or pseudo-tabes, belongs to this class, and is sufficiently common to be now recognised as a distinct entity. Muscular tremor, particularly in the morning, is perhaps one of the earliest signs of chronic tippling. In a patient whom I saw recently, there were several of the signs of disseminated sclerosis, *e.g.* nystagmus, tremor, and altered speech, but the circumstances which enabled me to differentiate the illness from

the classical disease which it simulated, were the history of the case, the extreme rapidity with which the symptoms had developed, and subsequently their rapid disappearance under treatment. In another patient, symptoms strongly suggestive of general paralysis presented themselves, but the youthful age of the patient, his well regulated movements, and the disappearance of the symptoms under total abstinence, demonstrated their functional character. Among the other effects of chronic alcoholism may be mentioned general or circumscribed œdema, also thrombosis of veins and albuminuria, which in time is followed by signs of interstitial nephritis. The heart too is apt to become dilated and the myocardium softened.

In the case of an acute illness in a child, or for the weak digestion of enfeebled infants, small doses of brandy may be temporarily beneficial. Children bear very large doses of alcohol badly, they quickly become comatose and die. A few ounces of pure whisky may throw a child of tender years into a state of stupor, in which he remains for two or three days, and dies without regaining consciousness; or the drowsiness, whilst persisting for days, is interrupted. There is spastic contraction of the limbs, unilateral or general convulsions, slight optic neuritis, with a normal temperature. In other cases, all the extremities are paralysed. The coma and convulsions thus induced in children closely resemble those observed in adults who are chronic drinkers, and in whom meningitis has developed. In the case of children, as in adults, the administration of alcohol for a lengthened period by parents, given with the view of strengthening them, is followed by gastric derangement, chronic intestinal catarrh, defective development, epileptic seizures, and subsequently by pathological changes in the liver, which ultimately lead to cirrhosis of that organ. Women who have children at the breast should be extremely abstemious as regards alcohol, for experience has shown that the intemperate use of spirits by mothers, when nursing, has caused their infants to become excited, and induced a train of symptoms not unlike those observed in meningitis.

There is an impression in the public mind that alcohol, in some way or another, prevents an individual catching infectious disease. It used to be stated, too, that if a man took spirits, he was able to do more muscular work, and that he endured cold better. The experience of our military authorities contradicts the second assertion, and that of Arctic explorers the third. In my Goulstonian lectures on lead poisoning, I confirm, by experiments upon animals, what clinical experience had suggested, so far as this form of industrial poisoning is concerned, namely, that lead workers who indulge in alcohol become a readier prey to plumbism than their more temperate mates. It is of the utmost importance that a definite opinion should, as far as possible, be expressed upon the question of whether alcohol has or has not any influence in preventing infectious disease. Abbott gives the details of numerous experiments which he carefully carried out upon rabbits, with the view of ascertaining how far alcohol protects animals against, or precipitates them into, infectious illnesses. The question, briefly put, is this: Is the normal vital resistance of an individual to infection by the common pathogenic bacteria favourably influenced by pure alcohol, and if so, does the fact hold good for beer, wines, etc. ? The experiments had reference principally to resistance to such organisms as the pyogenic cocci, the *Streptococcus pyogenes erysipelatis*, the *Staphylococcus pyogenes aureus*, and the *Bacillus coli communis*. Diluted alcohol was administered by intravenous injection; it was carefully measured, and administered in

quantities bearing a distinct relation to the weight of the animal and the symptoms of intoxication produced. Some of the animals were scarcely disturbed even by large doses, while in others, at the post-mortem examination, there were found such visible evidences of the effects of alcohol as acute gastritis, *e.g.* erosion and inflammation of the mucous membrane. Control experiments were made with animals to whom no alcohol was administered, the inoculations being the same in both. Abbott took six rabbits that were receiving alcohol daily in sufficient quantities to become intoxicated, and he inoculated them with bouillon cultures of the *Streptococcus pyogenes*, obtained from a phlegmonous inflammation in the human subject; at the same time he similarly inoculated five rabbits to whom no alcohol had been given. All the six rabbits died after losing weight, and they exhibited lesions referable to the inoculation (one of the animals showing, at the same time, in its liver the distinct effects of alcohol), while of the five inoculated non-alcoholic animals, only one died. Subsequently, he inoculated eighteen rabbits with suspensions of *Streptococcus pyogenes*. Of nine to whom alcohol had been administered, seven died with suppurative lesions; and as regards the other nine, to whom no alcohol had been given, no effect followed until the fifteenth day, when five died. His results obtained from suspensions of the *Bacillus coli communis* are not less interesting. They prove that, instead of fairly large doses of alcohol increasing the vital resistance to infectious disease, such tend not only to lower this resistance, but to increase the severity of the illness when caught. This opinion, arrived at as the result of experimentation upon animals, is quite in keeping with our clinical experience of how badly borne pneumonia, erysipelas, and other infectious diseases are by men who have been in the habit of consuming large quantities of alcohol daily.

Nor is there any truth in the opinion held by the laity, that the use of alcohol protects the individual against tuberculous disease. I do not refer to such a restricted employment of alcohol as a glass of beer or stout or a little wine at dinner time. That may be helpful to the individual. It is to the mistaken opinion that where there is a family predisposition to the disease, it is necessary to be somewhat more indulgent. In my experience of young men with a hereditary tendency to phthisis, alcohol has, by the late hours which it encourages, and the careless and irregular habits that it fosters, frequently precipitated the individual into active tuberculous disease, which abstinence and more careful living would assuredly have prevented. It indirectly favours the development of tuberculous disease. Pulmonary tuberculosis was found by Dickinson to be more frequent in drinkers than in ordinary people in the proportion of three to two. Rolleston, quoting H. Mackenzie, states that in sixty-seven cases of pulmonary tuberculosis occurring in drinkers, a family history of tubercle was only found in ten, whereas it is found in about 30 per cent. of the ordinary cases. The frequent association of pulmonary tuberculosis with alcoholic peripheral neuritis, and its presence, too, in nearly one-third of the cases of cirrhosis of the liver, are circumstances which show that under the debilitating influence of alcohol vital resistance is reduced, ordinary pulmonary catarrhs are not so quickly thrown off, and thus the bacillus of tubercle gains an easier entrance.

Diagnosis.—Now and again it has happened that an individual, found helpless and unconscious in the streets, and believed by the police to be drunk, has been taken to the lock-up and placed in the cells overnight, where he is found dead next morning. This has happened so

often, that in our large towns the casualty surgeon is more frequently called in than formerly to make a diagnosis in doubtful cases, for cerebral hæmorrhage, fractured skull, uræmic, diabetic, and epileptic coma have to be differentiated from acute alcoholic poisoning. The police cells are now in many cities warmed, so that death from lowering of the body temperature, which is one of the consequences of alcoholism, is less likely to occur, besides the inmates are usually visited at short intervals. A diagnosis is too frequently made simply from the alcoholic odour which hangs about an individual, but this is not enough; neither must a staggering gait, inability to stand, nor the use of obscene and violent language, be regarded as absolute proofs of drunkenness, for these may all be exhibited by a patient suffering from cerebral hæmorrhage. The urine should in all doubtful cases be examined for albumin and sugar, and the vomit for alcohol. As alcohol is eliminated by the kidneys, Anstie taught that an examination of the urine for alcohol might be a useful help, but although one drop of alcoholic urine will give, when added to 15 minims of chromic acid solution (1 in 300), a bright emerald-green colour, this cannot be regarded as absolute proof that a poisonous dose of alcohol has been taken. When taken in excess, alcohol is eliminated by the kidneys. Another test for alcohol is the production of iodoform. Heat the suspected liquid in a test tube with iodine and caustic potash, and if alcohol is present yellow crystals of iodoform will appear. So delicate is this test, that it will detect alcohol in the proportion of 1 in 10,000. Signs of fracture of the skull with depression of bone and of cerebral hæmorrhage should be carefully sought for. Coma may be present in cerebral hæmorrhage, and if the bleeding has occurred into the pons the pupils may be pin-point. I agree with Norman Kerr that "the only safe rule in such obscure cases is to treat the patient as suffering from an underlying and grave ailment, till the acute alcoholic symptoms have had time to disappear."

The diagnosis of *mania a potu* rests upon the history of recent drinking. Delirium tremens, on the other hand, may develop in people who have not been immediately drinking. No alcohol may have been taken for several days, and yet under the influence of an injury, exposure to cold, etc., an individual of intemperate habits may develop delirium tremens. To distinguish between alcoholic delirium and the excitement and wandering observed in pneumonia and specific fevers, the absence of rise of temperature and of dulness on percussion over the lungs would be important. But as a patient with pneumonia may also be the subject of delirium tremens, it is well to remember that acute delirium may last through the early part of the illness, and while it obviously increases the gravity of the illness, it does not necessarily follow that the case is absolutely hopeless.

The diagnosis of alcoholic neuritis is not always easy, for it frequently occurs in women of whose habits it is almost impossible to obtain an accurate history, even from their husbands, who too often are ignorant of the vice that is secretly indulged in. Alcoholic "foot-drop" and "wrist-drop" are distinguished from lead poisoning by the absence of a blue line on the gums, also by the history of painful sensations in the limbs, hyperæsthesia of skin, mental irritability, or enfeeblement. It is the presence of such sensory symptoms, and the fact of the illness being more slowly developed, that enable us to distinguish alcoholic neuritis from the acute spinal paralysis of Landry.

Paralysis due to alcoholic peripheral neuritis may persist for a long time and resist treatment, yet even apparently hopeless cases may in time

recover. For fully twelve months a male alcoholic paralytic occupied one of my beds in the Newcastle Infirmary. There was double ankle-drop, pointing of the toes, very marked atrophy of the legs, loss of knee-jerk, and extreme emaciation generally. The patient could neither stand nor walk, but by means of treatment, medicinal, electrical, and massage perseveringly followed, the disease was overcome, so that a little over a year after his admission he walked out of the hospital. The extreme emaciation of the limbs in alcoholic neuritis suggests progressive muscular atrophy, but in progressive muscular atrophy there is no sensory disturbance; besides, it is usually slower in its development, and the disease tends to affect the muscles of the hand and to create the deformity known as "*main en griffe.*" From acute anterior poliomyelitis it is distinguished by the paralysis being in this disease more complete, by sensory symptoms being absent, and by groups of muscles being simultaneously attacked, also by the fact of tenderness on pressure being more noticeable in alcoholic peripheral neuritis. Hysterical paralysis may be mistaken for alcoholic, but the loss of power, which in alcoholism is usually bilateral, is, along with distinct loss of sensation, unilateral in hysteria.

Much of the chronic invalidism seen in women who complain of frequent sensations of faintness, is the outcome of indulgence in alcohol. It is always a suspicious circumstance, where women lie in bed the greater part of the day, neglectful of domestic duties, and in whom no signs of real illness can be detected.

Prognosis.—With the exception of those patients whose coma is profound, or in cases where the severer forms of delirium tremens are ushered in by convulsions, and accompanied by a rise of temperature, and where excitement is accompanied by sleeplessness and inability to take food, where there are also albuminuria, rapid pulse, weak heart sounds, and signs of great prostration, the prognosis is favourable. Norman Kerr considers the recovery to be 90 per cent. The prognosis of uncomplicated alcoholic peripheral neuritis is also favourable, but in this and all other forms of alcoholism, it is a necessary part of the treatment that the use of spirits should be absolutely forbidden.

Treatment.—In very slight cases of delirium tremens, beyond withholding alcohol, the treatment is almost nil, for such cases tend to spontaneous cure. The treatment of the severer cases resolves itself into quieting the delirium, improving elimination and supporting strength. As the symptoms are due to a toxæmia, drugs given to induce sleep and quieten the nervous system must be administered carefully. Opium and morphine, in order to accomplish this, have to be given in rather large doses, and there is considerable risk in pushing them. This remark applies to all narcotics, particularly if the emunctories are inactive, and there is albumin in the urine. A hypodermic injection of hyoscin, $\frac{1}{150}$th or $\frac{1}{100}$th of a grain, may produce sleep, where morphia only causes excitement, but its effects must be watched. The application of cold to the head, a mixture of bromide of potassium, 40 grs., and of chloral, 20 grs., may be given, and repeated in an hour or two if necessary, or a mixture of potassium bromide, 20 grs., and tincture of hyoscyamus, $\frac{1}{2}$ oz., with ammonia and tinct. lupuli, or of pot. brom. and tinct. digitalis, is often serviceable. Other hypnotics, such as paraldehyde, urethan, sulphonal, or trional, may be given. All these drugs give best results when preceded by a free calomel purge. The administration of chloroform has been recommended, but its use is attended with danger. I have known it cause death. For the

acute delirium of a strong and well-built alcoholic subject, circumstances may be such, owing to the absence of sufficient personal help, that physical restraint of the individual may be necessary, *e.g.* placing him in a padded room, or the use of the strait-jacket. The employment of the strait-jacket, however, must be carefully watched. I have never seen any bad effects from the strait-jacket, but I am extremely careful to apply it only in uncomplicated cases, and then but for a very short time. Should an alcoholic patient who is suffering from delirium tremens develop in addition a pneumonia, and which a rise of temperature would suggest, the strait-jacket, if applied, would, by embarrassing the movements of the chest wall and pressing upon the false ribs, aggravate the pulmonary congestion, by forcing the respiration to become abdominal. The strength of the patient under all circumstances must be maintained, by means of strong soups, coffee, and milk, eggs beaten up with milk, etc. We are often asked should stimulants be given to alcoholic patients when there is evidence of the heart flagging and the pulse becoming weak? Friends of a patient will press this question upon the medical attendant, in the belief that it is in consequence of the sudden withdrawal of the usual stimulant to which the individual has been accustomed, that part of the illness is due. As the symptoms are consequent upon alcohol having poisoned the blood and deranged the nerve centres, we fail to see, on the theory of an existing toxæmia, how the withholding of the poison that created the illness can be the cause of the cerebral excitement. So far as prostration is concerned, usually this can be just as well met by stimulants other than alcoholic. I cannot remember a patient suffering from delirium tremens to whom I have been obliged to administer alcohol, but I would not refuse it if circumstances demanded it. Cardiac failure may be treated by hypodermic injections of spartein or of caffeine. It is always desirable to get the tongue cleaned, the emunctories kept active, and a taste for food established. When the patient begins to improve, strychnine nitrate is a useful tonic. Under its administration the craving for alcohol diminishes, so that in a few days it is completely gone. Under the combined influence, therefore, of abstinence from alcohol on the one hand, and the administration of strychnine on the other, the patient is soon restored to health; but, unfortunately, within the next few months there is perhaps a relapse, and it may be another attack of delirium tremens. In all cases it is necessary, where the delirium endures, that the patient should not be left alone, for, in the absence of the nurse or attendant, he may throw himself from a window, or resort to some other method of self-destruction. It is our duty to protect the individual against himself, as well as to prevent him from injuring others. It is during the first three or four days of the delirium that these accidents are most likely to occur.

It is all but impossible to prevent relapses on the part of alcoholics. The administration of strychnine, cinchona rubra, and the "gold" cure have each their advocates, but experience has shown that, while such patients can be restored to temporary health, their weakened will does not enable them to rise above temptation. Safety for them alone lies in total abstinence. An active out-door life, and removal of the individual from all causes of worry and from his boon-companions, temporary voluntary retirement to a retreat or to a home for inebriates, are recommendations the utility of which must be gauged by the particular case in question.

The chloride of gold just alluded to is administered hypodermically,

$\frac{1}{10}$th of a grain in 10 minims of water, thrice daily. It is regarded by some physicians as one of the best therapeutic agents in the treatment of chronic alcoholism, its action being similar to that of phosphorus and strychnine upon the brain and spinal cord. Patients have blamed the "gold" cure for a subsequent temporary impotency that is said to have arisen, but experience does not support this statement. Occasionally the arms swell in consequence of the repeated hypodermic injections, but this readily yields to rest and the application of a lead lotion.

MEAT OR PTOMAINE POISONING.

History.—For centuries men must have known that the ingestion of putrid food might be followed by serious consequences, but it was von Haller who, during the last century, first narrated how death followed the injection of an aqueous extract of putrescent meat into the veins of animals. In 1853, Stich showed that the administration of decomposing food caused intestinal catarrh, choleraic stools, staggering gait, convulsions, and death, without any lesion being found at the autopsy. Panum, three years later, determined the chemical nature of the poisons in putrefying food, and demonstrated their action upon the living body. Since then many investigators have been at work trying to solve the problems; but, as it was Selmi who first suggested the name ptomaine for the poison, so did he give an impetus to the study of the chemical processes involved in putrefaction. Selmi, however, did not succeed in isolating any single putrefactive alkaloid. This was reserved for Nencki in 1876, and it is to him we are indebted for the first chemical formula of a ptomaine. Brieger has isolated and determined the composition of many of these alkaloids, and has contributed largely to the literature of the subject. To the solution of the many chemical and bacteriological problems, which this form of poisoning raises, men like Vaughan, Novy, Hankin, Sidney Martin, Stevenson, Kanthack, Brouardel, Bouchard, and Gautier have devoted much of their time; but, in spite of the excellent work which these pathologists have accomplished, the subject of ptomaine poisoning remains one of considerable mystery.

Etiology.—The subject of meat poisoning is still one of such considerable obscurity and uncertainty, that it is impossible to speak dogmatically upon it. In the incriminated article of food there are frequently found micro-organisms and complex chemical compounds. These chemical bodies, since they are capable of combining with acids, resemble inorganic and vegetable bases. To them Selmi, an Italian toxicologist, gave the name of ptomaines, from the Greek word πτῶμα, a cadaver. Ptomaines are chemical bodies, basic in character, which develop in organic matter through the activity of bacteria, and since this is generally undergoing decomposition these products are on that account sometimes called putrefactive alkaloids. Usually formed during the early stages of decomposition, they are regarded by Vaughan and Novy as "transition products in the process of putrefaction, temporary forms through which matter passes, while it is being transformed by the activity of bacterial life from the organic to the inorganic state." Like vegetable alkaloids, they all contain nitrogen, but not all of them oxygen. The kind of ptomaine

formed during putrefaction must necessarily depend upon the particular bacterium present, the nature of the organic matter that is decomposing, and the conditions under which putrefaction is taking place. Bacteria were described by Pasteur as aërobic or anærobic, according as they grew best in the comparative presence or absence of air. Many micro-organisms flourish best when air is largely excluded, a circumstance which explains the multiplication of bacteria and the formation of ptomaines, in carcases buried some depth beneath the soil. While bacteria in all probability cannot live indefinitely without oxygen, yet their fermentative activity can be increased by reducing the oxygen supply, for the enzymes or chemical ferments which they form are capable of acting under anærobic conditions. Since ptomaines contain nitrogen, they are occasionally spoken of as bacterial proteids. Brieger and Fränkel called them "toxalbumins," and Neumeister "toxic proteins"; but as they are not all poisonous, and are not all albumins, but albumoses, globulins, nucleo-albumins, and peptones, it is simpler to retain the term ptomaine, so as to include all. Sidney Martin, Brieger, and Cohn have lately succeeded in removing all extraneous proteid material from these toxines, with the result that the product obtained is found to be neither an albumin nor a proteid. In the processes of fermentation there are concerned (*a*) bacteria, (*b*) the products of bacterial secretion and excretion, and (*c*) the secondary changes induced by these products.

The widely prevalent use of cheap tinned foods, while admittedly an enormous boon, is yet not without danger. It is estimated that 581,000 lb. of canned foods are consumed daily in this country. According to the American Bureau of Statistics, the export of canned beef alone was 63,698,180 lb. between June 1895 and June 1896. Brown of Bacup has collected and grouped the reports of cases of poisoning from canned foods that have appeared in the home medical journals from 1879 to 1897. Twelve deaths are reported. Canned meats and fish are responsible for these, since no fatal poisoning is known to have occurred from the use of canned fruits. In the case of tinned meats, *e.g.* mutton, beef, tongue, and rabbit, a ptomaine of bacterial origin probably underlies the poisoning, and this may have been produced in the meat (1) before it was canned, (2) after canning, or (3) after the tin is opened. In the preparation of the meat and during the steaming process, the toxic products of ptomaines if present may be rendered inert, but the nutritive value of the meat is lessened. Where ptomaines have formed, after canning, the gases produced by putrefaction cause a convex bulging of the ends of the can, to which the term "blown" is applied in the trade. When such a can is opened, the odour of putrefaction is so great that there can be no doubt as to the contents having become decomposed. Once a can of sound meat has been opened, it may be so acted upon by conditions of the atmosphere, that bacteria, finding a suitable nidus therein, rapidly multiply and form toxines, which are dangerous. Of fish, particularly salmon, this is especially true. Tinned salmon which exhibits a pale yellow colour, which is soft and friable, and therefore quite unlike the firm, red, and flaky muscle of the healthy fish, is risky. In the case of canned fruits the poisons are metallic, and arise from natural acids dissolving out of the solder tin, zinc, or lead. The longer canned fruit is allowed to remain in contact with an impure solder, the greater is the danger. All tinned meats should be eaten early, and should be kept in a cool place; when opened the contents should be transferred to an earthen-

ware vessel, and consumed within two or three days, according to the weather. "Blown" cans should be rejected.

Pathology.—Space forbids me enumerating all the bacteria that may be found in poisonous meat, but the following are known to have occurred: the *B. proteus, B. prodigiosus, B. subtilis, B. coli communis, B. termo,* and the *Staphylococcus pyogenes aureus.* As regards the kind of meat that has caused poisoning, Ballard has shown that of thirteen instances of meat poisoning, reported in England between 1880 and 1890, pig flesh was blameable in ten instances, veal in one, and beef also in one. As an illustration of the extent of this form of poisoning, the editor of the *British Medical Journal* states that during three months he received reports of cases of meat poisoning, implicating upwards of sixty people. Ballard believes that it is on account of pork yielding a larger proportion of gelatin, and affording therefore a more suitable medium for the cultivation of micro-organisms, that it is more dangerous,—an opinion which applies equally to veal. It is impossible to say what the mortality from meat poisoning definitely is. There must be many cases of ptomaine poisoning that are never diagnosed. Of people in regard to whose illness there has been no doubt, the death-rate has varied from 1·6 to 4·3 per cent., whilst in the severer forms of poisoning the illness has carried off 30 per cent. During 1893, in England and Wales, nine males and nine females died from ptomaine poisoning; and in 1894, seven males and ten females; while during 1895–96 the total deaths were nine and fourteen respectively. This cannot include all the cases, for there must be many obscure forms of septicæmia, pneumonia, and infective endocarditis, whose intestinal origin from decaying meat had never suggested itself. This was the case in the epidemic of pneumonia which so severely scourged Middlesborough a few years ago. It was not until the disease had existed some time, and its rate of mortality ran high, that Ballard traced it to the use of "American bacon."

As opposed to ptomaines, or the basic products of putrefaction, being the *materies morbi,* bacteriologists mention other basic substances, which, although the products of fermentative changes, are neither due to bacterial activity nor to retrograde metamorphosis. To such the term *leucomaines* is applied, a name given by Gautier from λευκώμα, meaning white of egg, to certain alkaloids which are formed in animal tissues during normal life. They are supposed to be continuously formed within the body, side by side with urea and carbonic acid, and at the expense of the nitrogenous elements. As they are found in the urine, Bouchard has sought for an explanation of their presence therein by supposing that their primary origin is the intestinal canal, from which they have been absorbed. It would appear, however, that the origin of leucomaines is more probably the metabolism of the nucleated cells of the body, and that they come under two distinct heads—(*a*) the uric acid, and (*b*) the creatinin group. Of these, *adenin,* which is present in the liver and urine of leucocythæmic patients, guanin, xanthin, and hypoxanthin may be mentioned. As the nucleus of a cell is the seat of considerable activity, it is nuclein that is regarded as the parent substance of adenin and guanin. Many of these alkaloids are extremely poisonous, so that health is only secured by the integrity and functional activity of the eliminating organs.

Extraction of ptomaines.—There are several methods of extracting these alkaloids, but all of them are surrounded by difficulties, owing to the fact that these basic substances rapidly undergo decomposition, and thus evade detection; they may be destroyed by the chemical

reagents employed; other complex compounds are frequently associated with, and not easily separated from them; and, finally, the reagents themselves, namely, alcohol, ether, etc., are not always pure. The Stas-Otto, Dragendorff's, Brieger's, Gautier, and Etard's methods are those chiefly used, but it is admitted that no perfect method has as yet been devised. As the methods are long and tedious, those who wish to follow out this part of the inquiry should consult such recent works as those by Vaughan and Novy, Farquharson and Gautier.

Symptoms.—When symptoms of poisoning have arisen after the ingestion of food, one of two things must have happened—(1) Either the food contained microbes which were present in the flesh of the animal at the time it was slaughtered, and were not destroyed by cooking; or (2) micro-organisms, subsequently to the death of the animal, found their way into the meat, and, as the result of their activity in either instance, toxic products were formed. Infection of the human body may thus occur from the entrance of disease germs or putrefactive bacteria, and, whilst these are the cause of the illness, the lesions, on the other hand, are generally less due to the presence of micro-organisms than to the action of their metabolic products. There is usually first an infection, and subsequently an intoxication, during which poison is being developed within the system as the result of bacterial activity; this confers upon the disease its specific and characteristic signs. Poisons which have been generated within the body of another animal may enter the human body through the alimentary canal by means of food. The difference between infection and intoxication is, that with infection there is a period of incubation, during which germs multiply before causing symptoms, while in intoxication symptoms develop almost immediately. The circumstance of a person dying shortly after eating a particular food, in which alkaloids are found capable of causing death when administered to animals, is an illustration of intoxication; but it would be infection if a bacillus was found, and if the meat when given to animals caused death after a definite time, corresponding to a period of incubation of from twelve to twenty-four hours. Opinion is still divided as to how far meat poisoning is to be regarded as an illness of an infectious nature like scarlet fever or tuberculosis, or whether it is due to cadaveric alkaloids, whose suspected existence in meat has not always been confirmed when submitted to chemical analysis. There are many pathologists who are sceptical upon these points, and who cannot accept the general application of the ptomaine theory. Among them is van Ermengen, who, basing his opinion upon a recent epidemic of poisoning by meat at Moorseele, has arrived at the conclusion that this form of poisoning arises from two sources—(1) Eating the flesh of animals killed during illness, and (2) the use of made-up dishes, hashed meat, pies, sausages, etc., in the manufacture of which, as for example, during the process of mincing and mixing, portions of internal viscera have slipped in, such as spleen, liver, lungs, kidneys, or intestine. It is in these organs of an animal which has died of an acute infectious malady, that micro-organisms and their toxines would most abundantly prevail. It is now several years since our attention was drawn to poisoning by sausages, an accident to which the term *botulisme* is applied. Meat undergoing putrefaction is justly condemned, but at first sight it seems scarcely credible that the flesh of very young healthy animals should favour auto-intoxication. It is Charrin's opinion that auto-infection of man may arise from the micro-organisms which normally inhabit his intestine having their

virulence increased by toxic materials, introduced by food that is beginning to decompose. According to him, veal constitutes in the digestive canal a gelatinised pulp, which is highly favourable to the multiplication of the intestinal bacteria.

After the ingestion of meat containing micro-organisms, present in the flesh of an animal when it died, several hours or a day or two may elapse before symptoms appear. There is a period of incubation similar to that in infectious diseases. When meat is eaten that has been invaded by microbes subsequent to the slaughter of the animal, there is generally a period of incubation. In such a case, there is probably associated with the bacteria the toxines they have formed; and if so, symptoms of toxæmia will rapidly show themselves, followed sooner or later by those of the infective disease. Where meat contains only alkaloids or ptomaines, the symptoms are those of chemical poisoning, and these may appear shortly after eating the food, or be delayed for several hours.

Infectious disease may arise in various ways. Certain microbes are known to be poisonous to the human body. They produce chemical ferments therein, or form chemical poisons by splitting up pre-existing compounds. The entrance into the system of micro-organisms will not only cause disease, but confer upon the disease an infectious character. Microbes multiply and elaborate chemical compounds within the system, which are capable of inducing particular effects. It is sometimes difficult to distinguish between symptoms due to infection and those consequent upon chemical poisoning. The symptoms of the latter occasionally resemble those observed in acute gastro-enteritis, namely, purging, vomiting, cramps in the legs, an elevated or subnormal temperature, followed by death within a few days. Given a case where poisoned meat has been eaten, it is impossible to say what symptoms, if any, will follow. Much depends upon the particular bacterium, the organic medium it is developing in, the stage of putrefaction reached, and the resistance or idiosyncrasy of the individual. The symptoms would probably be in succession—(1) gastro-intestinal, (2) nervous, (3) cardiac, (4) skin eruptions, (5) inflammation of serous membranes, and (6) albuminuria; but the period at which these show themselves varies, owing to the fact that, while the illness might begin as an infection, it is usually followed by an intoxication, consequent upon absorption of the products elaborated by the micro-organisms. Bacteria are thus able to act in a double way through their own secretions. Gautier and Etard have shown that during putrefaction the acid reaction which is present in the experimental tube during the first few days, and which is due to the presence of lactic acid, becomes replaced by a reaction that is alkaline. It is at this stage that there appears a series of basic alkaloids, like choline and neurine (Brieger), the latter being extremely toxic, and differing from choline in containing one molecule less of water; subsequently, that there arise neuridine, parvoline, collidine or hydrocollidine (Pouchet), bodies which possess strong convulsive properties, and which determine effects similar to those of muscarine, namely, salivation, dyspnœa, respiratory weakness, and cardiac failure, and which, since they are capable of having their effects neutralised by atropine, are occasionally called ptomatropine.

One of the earliest illustrations in this country of the bad effects arising from eating ham containing toxines from putrefaction was the Welbeck poisoning case. In June 1880 there was a sale of timber and machinery on the estate of the Duke of Portland, at Welbeck. The sale

lasted four days, and was attended by a large number of people. Luncheons were served in a neighbouring hotel, and consisted of cold boiled ham, cold boiled and roasted beef, cold beef-steak pie, bread, cheese, pickles, and chutney sauce. The drinks were bottled, and draught beer, spirits, ginger-beer, lemonade, and water. Seventy-four people were poisoned, of whom four died. Ballard, in investigating the outbreak, reported that diarrhœa was one of the most common symptoms, that a period of incubation preceded the illness, varying from twelve to forty-eight hours; that whereas in some the symptoms developed suddenly, in others there was an incubation period, during which there were languor, loss of appetite, nausea, fugitive abdominal pains, followed by a sense of chilliness or distinct rigors, giddiness, faintness, staggering gait, headache, cold clammy sweats, difficulty of swallowing, vomiting, and diarrhœa. Extreme debility was one of the most characteristic symptoms. The temperature ranged from 99° to 104° F., and the pulse from 88 to 128. In the fatal cases death was preceded by collapse and by signs not unlike those of cholera, namely, cyanosis and coldness of the extremities. Ballard traced the illness to the hams that had been eaten. Klein found in them a bacillus, cultures of which, when inoculated into animals, were followed by pneumonia. The Welbeck case demonstrates what so frequently happens, namely, that toxines give rise to different symptoms in different people, partly owing to the fact that there may be more than one toxine present in the meat, and that they are not evenly distributed throughout the carcase of the animal. It is thus that we seek to explain, not only the variability of the symptoms, but the negative results that follow the subjection of meat to a chemical or bacteriological examination, for the most poisonous parts of the food may already have been eaten. Death may follow the ingestion of decomposing meat, and yet careful examination, conducted by skilful analysts, may fail to detect the alkaloids that caused the poisoning, owing to the ptomaines in the process of analysis becoming split up into non-poisonous bodies, and also, as Dixon Mann believes, owing to such poisoning being the joint result of the bacteria and their formed ferments. Many so-called toxines are not basic products at all, but toxalbumoses, and of these we know little beyond the fact that they are unstable bodies, not crystallisable, whose presence is only indicated by the characteristic effects which they produce upon animals. Besides, there is an individual as well as a racial idiosyncrasy to such poison. A disagreeable odour emanating from meat is no doubt more or less significant. There is a stage in the putrefaction of meat which is dangerous, yet if decomposition is allowed to proceed further, the danger disappears. On the other hand, the flesh of an animal slaughtered on account of illness may be eaten with impunity immediately after death, but if kept for a few days it may become toxic. The flesh of animals that are suffering from such septic diseases as hæmorrhagic enteritis, multiple arthritis, post-partum metritis, etc., is, if the animals are killed *in extremis*, always more dangerous than if destroyed in the earlier stages of the illness. It is not to be inferred from this, however, that absolute safety is obtained by early slaughtering. Basenau mentions an experiment carried out in the slaughter-house at Rotterdam, where an ox was inoculated in the jugular vein with a culture containing bacilli got from a meat-poisoning case. The animal was killed twenty minutes after the inoculation, and while at first only a few bacilli were found in its blood, liver, and spleen, these micro-organisms rapidly increased in number within a few hours.

As only very few bacilli were found in the muscular tissue of the animal, it was presumed that if eaten early little risk attended the use of it. Fifty-three persons resolved to try it; of these, fifteen became ill with headache and diarrhœa after a lapse of twelve to eighteen hours, but all recovered. Those who do not accept the ptomaine theory of meat poisoning support their arguments by appealing to facts that are well known to most of us. In our large towns, late on a Saturday evening, it is no uncommon sight to see crowds of poor people around a butcher's or a poulterer's stall, bidding for meat, fish, and game that are already in an advanced stage of decomposition. These people do not seem to suffer any inconvenience from eating such, but rather thrive upon it. Oriental people also appear to be indifferent to the wholesomeness of their food. According to Novarre, rotten fish constitutes the food by preference of millions of Indians, Indo-Chinese, Malayans, Polynesians, and Negroes, who nourish themselves upon this mess, even preferring it when decomposition is most advanced. The taste of many British sportsmen lies in the same direction; they like their game "high." It is fortunate that the gastric juice, in addition to being a digestive, is also antiseptic, otherwise serious consequences would oftener follow. With these facts before us, the question naturally arises, whether putrefaction, pure and simple, can be held responsible for the illness that follows the eating of decayed meats. In an epidemic at Frankenhausen, carefully investigated by Gärtner, the meat did not present the slightest appearance of putrid change. Again, microorganisms and ptomaines may be present in meat, and as to their virulence there may be no doubt, but it is scarcely fair to argue, when these substances have been injected into the subcutaneous tissues, the veins or peritoneal sac of animals, and symptoms have followed, that poisoning would have been induced had the same substances been administered by the alimentary canal. When introduced into the body by this channel, many of these substances lose their poisonous properties, and in order to produce their effects it is necessary to give them in larger quantities. This argument covers only part of the ground, however, for some animals are refractory to certain poisonous foods when taken by the stomach, whilst others suffer equally with men, whether the poison enters by the alimentary canal or by intravenous injection. In the human subject there is a similar idiosyncrasy, so that while some people can eat decomposing meat, and hardly suffer, others are made seriously ill or die. It is difficult to explain the variation of symptoms in different people. Wiedner relates that of ninety people who were ill through eating roast goose, some suffered from pain in the abdomen and vomiting; others had diarrhœa; in some the symptoms were those of cholera nostras; in others there were cramp-like pains in the muscles of the extremities and neck. Toxine poisoning may follow the ingestion of meat, which exhibited no trace of putrefaction at the time it was eaten. It may have contained bacilli, capable of producing ptomaines. On the other hand, toxic meat may lose its poisonous properties as putrefaction advances, not so much from bacteria dying off, as in consequence of an alteration in the products of decomposition they lose their poisonous properties. Klein found a bacillus in some fresh meat-pie which had made several people ill, and which caused death when given to mice. After keeping the pie for several days, by which time an intensely putrefactive odour had developed, it was found to have lost its poisonous properties, for mice now fed upon it no longer suffered. Cooking usually destroys both the micro-organisms and their poisonous alkaloids, but just

as the spores of certain bacteria are capable of resisting great heat, so some toxines are similarly endowed with the capability of resisting temperatures that are fatal to micro-organisms. Once meat has become impregnated with ptomaines, there is no certainty that cooking will ever render the flesh harmless. There may be no disagreeable odour arising from it. Flesh meat that yields either a sweet or a sour odour, without anything of the nature of putrefaction about it, is, however, often more dangerous than that which is decomposing. This is probably owing to the fact that the more poisonous toxalbumoses are formed in the earliest stages of putrefaction by bacteria, at a time prior to that in which a more general disintegration of tissue proteid takes place, whereby, as decomposition advances, ptomaines are formed, some of which only are poisonous. Meat which was perfectly safe when eaten warm may change after cooling and keeping. It may then become the arena of bacterial activity, and the seat of the formation of alkaloids. A few years ago I was called to the Newcastle Industrial Schools, to deal with an outbreak of diarrhœa, which had suddenly developed. Nearly the whole school had been stricken. Two days previously the inmates had enjoyed their Sunday's dinner of roast beef. The meat left over was warmed up and eaten on the following day. On the Tuesday morning there was an epidemic of diarrhœa, upwards of a hundred lads being ill. Those children who had not partaken of the warmed-up meat, although placed under the same dietetic conditions, except as regards this one particular meal, alone escaped. In keeping cold cooked meat for a few days, risk is sometimes run, for during this period it may become contaminated, owing to the fact that some bacteria multiply at a very low temperature, 32° F. The circumstance of the meat having been kept even in an ice safe is no absolute guarantee against the possibility of bacterial invasion. The air of an ice chamber should be free as far as possible from moisture, and the meat kept dry as well as cold, for only thus can it remain fresh. The drawback to the use of the cooked pies that are sold in shops, of sausages, pickled meats, etc., is that we have no proof of the soundness of the meat employed in their manufacture. Unsound meat is sometimes pickled in the hope of getting rid of an unpleasant odour, but this does not remove the poisonous alkaloids. The muscle of meat is always less dangerous than any of the internal organs.

We know that risk is incurred by eating putrid fish, but poisoning may follow the ingestion of fresh fish, lobster, crab, and oysters, for these may have acquired poisonous properties from the medium in which they were caught, as for example water adulterated by the sewage of towns or polluted by factory refuse. Oysters reared near the mouth of rivers contaminated by the sewage of towns have caused illness resembling typhoid fever. The fatal illnesses that followed the ingestion of oysters at the Stirling County Ball a winter or two ago were a convincing demonstration of the virulent effects of poisons that may be locked up within this edible bivalve. Similar effects have followed the eating of tinned salmon, sardines, etc. Admitting that the fish were healthy when placed in the tin, once this is opened and kept exposed to the air certain changes may occur which render the contents extremely poisonous. Symptoms rapidly develop after eating such fish, except in the case of oysters, when there is usually greater delay; and while the symptoms vary in accordance with the cause and the idiosyncrasy of the patient, fever is not, as a rule, present, nor is there diarrhœa, but rather constipation, tenesmus, and bloody evacuations. Usually there are vomiting, cardiac and respiratory distress, nervous symp-

toms, perspiration, and contracted pupils, along with erythema or urticaria, particularly in poisoning by crab. In oyster poisoning, symptoms are more slowly developed, and these are indigestion, with a feeling of faintness, followed by nervous symptoms, and frequently accompanied by erythematous patches in the skin, or by intense itching. From toxic mussels, Brieger, Salkowaki, and Seeger obtained an alkaloid, known as mytiloxine. This substance acts like curari, but has in addition the power of contracting the pupil. Brieger obtained from decaying fish, ptomato-muscarine; Boklisch from putrefying perch got guanadine; whilst Gautier and Etard have isolated a series of toxic bases, *e.g.* hydrocollidine, which produces convulsions and causes death, with the heart arrested in diastole; parvoline and muscarine; and from cod-liver oil trimethylamine. Mydaleine, obtained from the human cadaver, causes, when injected into animals, the symptoms of alkaloidal poisoning, with, in addition, a rise of temperature, dilatation of the pupils, and a tendency to paralysis and convulsions.

Milk, cheese, and butter may cause poisoning. Milk may contain deleterious material owing to the animal which supplies it having previously eaten some metallic poison, or injurious plants. It may also contain microorganisms, such as the tubercle or typhoid fever bacillus. Cheese may undergo putrefaction and develop such toxic alkaloids as tyrotoxine (Vaughan), trimethylamine, neuridine, and toxalbumins. The symptoms which these cause differ little from those already described, except that in addition there is diplopia, as mentioned by Teissier. Poisoning by butter is not unknown. Sir Charles Cameron states that in a family which had breakfasted upon bread, butter, and tea, all the members with one exception suffered from choleraic diarrhœa. The individual who escaped had refused to eat the butter, on account of its intense rancidity. So severe were the symptoms, that one of the children died. In another instance a family developed choleraic diarrhœa. All the members had eaten very rancid butter, and all suffered. In the butter, on analysis, there were found ptomaines in large quantity.

Scurvy, hitherto believed to be caused by the absence of fresh vegetables in the dietary, is now considered to be dependent upon the consumption of tainted and salted meat.

Diagnosis.—The illness is one of sudden development. Usually several healthy people are simultaneously seized, and there is a history of a particular kind of food having been eaten. There may, however, be a period of incubation, either of hours or of a few days; only a few hours if it is alkaloidal poisoning, a few days if it is infection. The latter will depend upon the kind and number of the micro-organisms. In the Middlesborough epidemic of pneumonia the period of incubation varied from eighteen to thirty-six hours. The symptoms originating in the alimentary tract are followed by those of the nervous system; there is extreme exhaustion, free perspiration, and a tendency to respiratory and cardiac failure. Since bone marrow is acknowledged to form a good resting-place for micro-organisms, these may find their way thereto from the intestinal tract and set up an osteomyelitis, which can only thus be explained.

Prognosis.—The prognosis is grave in most cases, but it is relative to the character of the symptoms. Repeated vomiting and diarrhœa, nervous phenomena, extreme muscular debility, and albuminuria, indicate rather a severe type of meat poisoning.

Treatment.—Abolition of private slaughter-houses and a careful

examination of the carcases of animals by a skilled public officer; prohibition of the use of the flesh of animals killed on account of puerperal septicæmia and other blood diseases; also those that have died from acute enteritis and pneumo-enteritis; such strict supervision of the lower class of butchers, that, under heavy penalties, it will be impossible for them to sell or convert suspected meat into hams, sausages, and pies. Absolute security, however, cannot be obtained. We must rely to a very large extent upon the honesty and the care exercised in the buying and selling of meat by our butchers, and of the integrity of sausage-makers, so that they will not include in the manufactured articles portions of the internal organs of animals slaughtered for disease. Scrupulous cleanliness all round is a necessity, not only of the hands of those who cut up the meat, but of the rooms in which it is kept and disposed of,—rooms which should be cool, well ventilated, and far removed from drains and all chance of contamination by sewer gas. Tinned meats should be examined before being eaten, and all tins should be rejected if they have been bruised, "blown," or opened in their transit. Those, too, should be rejected, the jelly of which, when exposed, is found to have become liquefied, or from which a putrefactive odour is escaping. Milk that might contain tubercle bacilli should be boiled.

In meat-poisoning the period which elapses between the ingestion of the food and the appearance of the symptoms is a point of importance. The early development of symptoms indicates intoxication due to one or several ptomaines, whereas if delayed for twelve or fifteen hours it suggests the probability of microbial infection; but again I repeat, that this distinction is not absolute, although quite sufficient for a fair inference to be drawn between ptomaine and bacterial poisoning, and to be a guide as regards treatment. When gastric symptoms appear early, an attempt should be made to empty the stomach by emetics, or the stomach-pump, or to clear out the intestinal tract by cathartics, in the hope of preventing further absorption. In a case of bacterial infection without diarrhœa, a gentle purgative like castor-oil can do no harm. A solution of tannin is recommended, on the ground that it precipitates alkaloids, but we still require proof of its utility. We should try to render the contents of the · intestine aseptic, and prevent if possible the multiplication of germs therein. Bouchard, Lauder Brunton, and others have shown what excellent results follow a rigid intestinal antisepsis. The salicylate of soda, by promoting the flow of bile which is itself antiseptic and an aid to intestinal peristalsis, is worthy of a trial if the patient is already not too much depressed. Of the efficacy of naphthol-beta and salol, I can speak most approvingly, as also of sulpho-carbolate of soda in 15 to 30 gr. doses three or four times a day. Next to intestinal antisepsis comes antidotal treatment, if the particular alkaloid can be determined. Several of these alkaloids behave like muscarine, and cause, among other symptoms, contraction of the pupil. Atropine is the antidote to such alkaloids; it may be administered subcutaneously in from $\frac{1}{120}$ to $\frac{1}{60}$ gr., and repeated within half an hour if necessary. Some ptomaines, on the other hand, behave like atropine, and cause dryness of the throat, increased intestinal peristalsis, and dilatation of the pupil. Their influence should be combated by subcutaneous injection of morphine or small doses of pilocarpine. For the remainder, symptoms must be treated as they arise—convulsions may be treated by potassium bromide; faintness by ether, ammonia, caffeine, or strophanthus; vomiting, if excessive, by sinapisms to the epigastrium, or

internally by ice and effervescing mixtures; pyrexia, by quinine or salicylate of soda; constipation, by mild purgatives; whilst diarrhœa, if not profuse, is best left alone. We seek to favour elimination by the kidneys and skin, and, above all, we maintain the strength of the patient by stimulants, milk, strong animal soups, and concentrated but easily digested foods.

POISONING BY VEGETABLE ALKALOIDS AND OTHER ACTIVE PRINCIPLES.

WE apply the term alkaloids to substances of a basic nature formed in the tissues of plants or animals, and which are capable, like alkalies, of combining with acids to form salts. It is to these bases that plants owe their physiological properties. They contain carbon, hydrogen, and nitrogen, and all of them oxygen, with the exception of conine, nicotine, and spartein. Extremely complex in their chemical composition, alkaloids have been grouped with the amines or amides, ammonia substances, one or two of whose hydrogen atoms have been replaced by a radicle. One of the principal characteristics of the group is instability. They readily decompose under the influence of temperature and oxidising agents, but particularly when acted upon by micro-organisms. It is thus that, after death from alkaloidal poisoning, the alkaloid itself may disappear from the body through decomposition; hence the necessity, in a suspected case of this form of poisoning, for examining the body shortly after death.

History.—The discovery of alkaloids marks an important step in chemistry and therapeutics. Formerly it was believed that vegetables contained only a few organic acids, but Derosne, when investigating certain medicinal plants in 1803, discovered a substance with an alkaline reaction, to which he gave the name of opium salt, and which in 1804 was recognised by Sertüner as morphine. Since then, by improved chemical methods, numerous alkaloids have been added to the list; these retain as their terminals the letters *ine*, *e.g.* morphine; whereas, for non-alkaloidal active principles, the letters *inum* or *in* are generally employed, as in digitalinum and digitalin. The simplest chemical compound belonging to the group of ring-formed atomic complexes, *i.e.* substances which contain carbon and hydrogen, but in which the ring is capable of being closed by an atom of nitrogen, is pyridine, a product obtained from coal tar. All alkaloids obtained from plants that act injuriously upon the human body, are modifications of pyridine. Our knowledge of the atomic relationships of pyridine has enabled the chemist to synthetically form various alkaloids.

Etiology and symptoms.—The part played by alkaloids in the functional life of plants is not known. More than one alkaloid may be found in the same plant; and while many of these are extremely virulent poisons, others are innocuous. It is characteristic of them, as opposed to mineral poisons, that they produce symptoms almost immediately after entering the system—symptoms which run a rapid course, and with increasing severity. To this rule there are exceptions, as witness the tardy development of symptoms in morphine poisoning. Nearly all alkaloids exert their baneful influence upon the nervous system. In some instances there is also considerable derangement of the digestive tract. As regards reaction to alkaloids, there is not only in the human subject but in

animals a varying susceptibility. This idiosyncrasy in man is shown by the manner in which some people are influenced by minute doses of morphine and quinine compared to others, and in animals by the susceptibility of the dog, for example, to minute doses of atropine, whilst upon rabbits the drug is practically harmless. Experimental data thus obtained are not therefore of general application. The intensity of the action of alkaloids is largely dependent upon the complexity of their molecular structure and the sum of their atomic weights; on the other hand, the rapidity with which their physiological effects are produced is dependent upon their easy transition from complex to simpler bodies. The effects, too, are largely determined by the purity of the alkaloid and the development of the nervous system of the victim. The nervous symptoms are proportional to the organisation of the animal, and as in some animals certain parts of the nervous system are more highly developed than others, so are the effects of alkaloidal poisoning correspondingly exhibited by the spinal cord or the cerebrum.

Space only allows of our mentioning a few of the principal vegetable alkaloids, and their physiological effects; but before doing so we may briefly allude to the general lines of treatment to be followed in cases of alkaloidal poisoning. In order to be successful, the patient requires to be seen early, and the stomach washed out at once. Where this is impossible, we may administer substances to render the alkaloid less soluble, and for this purpose, tannin, iodine dissolved in potassium iodide, or the administration of finely divided charcoal, which, by mechanically uniting with the poison, retards its absorption, are recommended. Once the poison has been absorbed, attention must be directed to the more serious symptoms, depending upon implication of the nervous system, and which require to be met by such drugs as chloral, chloroform, ammonia, and caffeine.

Aconitine poisoning is rare. The usual symptoms are numbness and tingling in the lips, tongue, and throat, burning pain in stomach, nausea, and vomiting. So benumbed are the mouth and throat, that swallowing becomes almost impossible. There is cold perspiration, feeble heart's action, extreme prostration, and death from syncope, occasionally preceded by convulsions and delirium. Aconitine is one of the most active and rapid poisons with which we are acquainted. One sixteenth of a grain ($\frac{1}{16}$) has caused death in a few minutes. In the body, after death, there are no pathological appearances that are either constant or conclusive.

In **atropine poisoning** the symptoms usually begin within an hour of swallowing the poison, and consist of great dryness of mouth and throat, difficulty of swallowing, imperfect vision with very dilated pupils, delirium, difficult articulation, feeble, rapid, and intermittent pulse, reddening of skin, coma and convulsions. The quantity of atropine required to cause death depends upon the channel of its administration. Half a grain given by the mouth has caused death, and $\frac{1}{30}$ of a grain administered hypodermically. Recovery from large doses has taken place. The principal post-mortem appearances are dilated pupils, hyperæmia of mucous membrane of stomach and intestines, congested lungs, and empty heart. The treatment for atropine poisoning, in addition to that already mentioned on general lines, is the hypodermic injection of morphine in $\frac{1}{4}$-gr. doses from time to time. As the alkaloid is eliminated by the kidneys, it is well to catheterise the bladder, not only on account of retention, which is fre-

quently present, but to prevent reabsorption of the atropine from the bladder.

Cocaine.—The alkaloid of *Erythroxylon coca* is employed in medicine in the form of hydrochlorate. It is used as a local anæsthetic, particularly for mucous surfaces, as it acts upon the peripheral terminations of sensory nerves. Like caffeine, it removes, when taken internally, the sense of muscular fatigue. Most cases of cocaine poisoning have arisen from the application of the alkaloid to mucous membranes. Alarming symptoms have sometimes suddenly shown themselves in patients when in the dentist's or laryngologist's chair, owing to cocaine having been injected into their gums, or when employed as a spray to the throat. The symptoms are nervous excitement, followed by a very rapid pulse and extreme difficulty of breathing, during which the individual becomes markedly cyanosed, and the pulse so feeble as to be almost imperceptible, coldness of the extremities, and, if the dose has been large, convulsions, coma, and death, from apnœa or syncope. The most frequent and alarming symptom is altered respiration, but the drug apparently operates *seriatim* upon cerebrum, medulla, and spinal cord. Cocaine acts with extreme rapidity—it has caused death within one minute. Severe and rapid as the symptoms usually are, there is hope of ultimate recovery if the patient survive half an hour. A very small dose, administered hypodermically, *e.g.* $\frac{1}{12}$ gr., or if applied locally $\frac{1}{2}$ gr., may cause death; but recovery may follow such large doses as 3 or 4 grs., if the cocaine has been taken by the mouth in solid form. There are no characteristic post-mortem appearances observed in this form of poisoning.

Nicotine or tobacco poisoning, although an extremely fatal poison, has caused very few deaths. The symptoms are giddiness, exhaustion, tremor, nausea, vomiting, feeble circulation, and fainting, difficult breathing, accompanied by convulsions and followed by coma, death taking place by apnœa, the heart beating after the breathing has ceased. Formerly tobacco juice and leaves used to be applied to ulcers, but violent and even fatal symptoms are known to have followed their application. Such symptoms, too, were observed after the administration of tobacco infusion by enemata given to patients suffering from dislocations, in the days before chloroform, to overcome muscular spasm. Many people have a marked intolerance of tobacco. In the act of smoking, nicotine is developed; by far the largest part of this, however, is destroyed, and its place taken by less harmful products of combustion, such as the pyridine bases, otherwise, unpleasant symptoms would be much more frequent. Pyridine was found by Hare to be a respiratory paralysant and depressor of the spinal cord. Less than a grain of pure nicotine has caused death. There are no characteristic post-mortem appearances. In addition to the general treatment, it may be necessary to maintain respiration by electricity and the inhalation of oxygen.

With the impairment of vision consequent upon tobacco-smoking, medical men have long been familiar. The central field of vision is principally affected, causing colour-blindness for red and green. Tobacco has a special preference for the optic nerve, and especially for its peripheral terminations. In some patients, Judson Bury has observed loss of power in fingers and wrists, accompanied by loss of cutaneous sensibility. He is inclined to regard tobacco as capable of inducing peripheral neuritis. Considerable discrepancy prevails as to the quantity of tobacco necessary to produce deleterious effects. De Schweinitz is correct when he says

much depends not only upon the quantity, but also upon the quality, of the tobacco, the idiosyncrasy of the patient, and the relation of the smoking to the taking of meals, the effects being more likely to be induced on an empty stomach, and especially if the tobacco smoke is inhaled. French tobacco contains, according to Schlösing, 5 to 8 per cent. of nicotine, Virginian tobacco 6 to 7 per cent., Maryland and Havana 2 per cent. Turkish tobacco is said to contain only from 0·75 to 1·25 per cent. of nicotine.

Morphine is the most important of the several alkaloids obtained from *Papaver somniferum*. It is a strong narcotic. All the alkaloids—morphine, codeine, narcotine, paverine, and thebaine—are combined in opium with meconic acid. These alkaloids are not all alike in their action. Some, like morphine, have a narcotising action, namely, narceine, codeine, and papaverine; whilst others, such as thebaine and narcotine, exercise a convulsant influence. Morphine is usually regarded as having from four to six times the activity of opium; besides, it is more soluble in the secretions of the stomach. Shortly after its absorption the individual becomes somewhat dizzy, and is seized with an irresistible inclination to sleep. The nervous system is profoundly affected; the respiratory centre is deranged, judging from the slow and laboured breathing, which may be not more than two or three times to the minute; the pulse is feeble; the pupils, at first extremely contracted, may dilate; the intellect is confused; and there is mental stupor, which deepens and is accompanied by increasing muscular weakness. Respiration becomes more difficult, and finally ceases, although the fatal termination frequently comes, and quite unexpectedly too, from cardiac failure. Symptoms of poisoning may show themselves shortly after morphine has been taken, or they may be delayed for an hour or two; but once they appear the tendency is for them to increase in severity. One grain of morphine taken by the mouth has caused death, and $\frac{1}{3}$ gr. administered hypodermically has caused serious symptoms. As the drug is one toward which people exhibit a varying idiosyncrasy, the symptoms, both as regards the time of their appearance and severity, will be largely influenced by the susceptibility, vigour, and good health of the individual. Apoplectic and uræmic coma, acute alcoholism, and poisoning by chloral and other narcotics, may be mistaken for morphine poisoning. Sometimes it is extremely difficult to differentiate one from the other. The history of the case, and the finding of a bottle that has contained morphine, the extremely contracted pupils, the odour of the breath and the rapid development of symptoms in the absence of signs of ill health, are a help in the diagnosis, though not infallible guides. There are no post-mortem signs characteristic of morphine poisoning. As regards the other alkaloids obtained from opium, codeine resembles morphine in its action; narceine is a hypnotic; narcotine, in addition to being slightly hypnotic, is strongly convulsant; whilst thebaine causes convulsions, and is therefore not unlike strychnine in its action. It is owing to the numerous alkaloids which the crude drug contains that opium has such a complicated action upon the body.

Strychnine. — Most organic compounds, when treated with sulphuric acid, are so destroyed that they can be no longer identified; but it is characteristic of strychnine that it resists the action of this acid. This circumstance affords a valuable means for separating strychnine from other organic substances. The alkaloid has an extremely bitter taste. It can be tasted in 70,000 parts of water. Symptoms usually appear within ten minutes after a toxic dose has been taken; but these

may be deferred if the stomach contains food, or they may appear very early if the drug has been administered hypodermically, when $\frac{1}{4}$ gr. may prove fatal. It is stated that if a patient suffering from strychnine poisoning survive three to four hours, his chance of recovery is good; but this cannot altogether be relied upon, for death has supervened eighteen hours after the development of the symptoms. It is difficult to say what is the action of strychnine upon the system, but it seems to heighten the reflex excitability of the spinal cord by reducing the resistance in the paths along which impulses travel, so that on the slightest sensory impression being made, for example, simply touching the bedclothes, the individual is thrown into a tetanic convulsion amounting at times to opisthotonos, the legs being extended, the feet arched, and the head thrown violently backwards, so that the body practically rests upon the heels and occiput. The respiratory muscles, too, are thrown into such a state of spasm that breathing becomes impossible; whilst the feeble, irregular pulse, dilated pupils, and cyanotic face indicate the extent to which aëration of the blood is checked. Once the convulsion has subsided, and the muscles have become relaxed, the body is found to be covered with cold perspiration, and the patient, overcome by exhaustion, falls asleep. After a varying interval, the convulsive paroxysms reappear. Reflex excitability is so heightened that a loud sound or a touch may cause a convulsion; and as the intellect remains clear, the patient, conscious of the terrible ordeal he has passed through, and dreading its repetition, pleads anxiously for relief. Death frequently takes place during a convulsion.

With the exception of tetanus, there is no disease that exactly simulates strychnine poisoning, although in courts of law, epileptic, uræmic, and puerperal eclamptic convulsions have been suggested as resembling it. There are few medical practitioners who would mistake either of these for strychnine poisoning. So far as tetanus is concerned, there is usually the history of an injury; and besides, tetanus is usually slowly developed, is gradually progressive, and has nothing of the acute urgency of symptoms about it so characteristic of the alkaloidal poisoning. In tetanus, too, it is the muscles of the back of the neck and jaw that are first affected, giving rise to the characteristic "sardonic grin"; whereas in strychnine poisoning the muscles of the extremities are first affected, and the muscles of the neck and jaw last. In tetanus, in addition, there is a greater tendency for rigidity to persist between the spasms. Some writers maintain that the temperature is higher; but this latter is not a reliable sign. The only post-mortem sign of value in strychnine poisoning is the continued rigidity of the muscles, which lasts for a lengthened period. If, along with this, there are signs of congestion of the brain and spinal cord, with subarachnoid effusion, the diagnosis of strychnine poisoning is corroborated.

Digitalin.—When acted upon by dilute hydrochloric or sulphuric acid, it decomposes, forming a glucose; hence it is sometimes spoken of as a glucoside. The therapeutical properties of the plant *Digitalis purpurea* depend upon digitalin and digitoxin, and of these the former is the more important. It slows the action of the heart, and in toxic doses may arrest it in diastole. In medium doses, it at first accelerates and then retards the beat of the heart; it causes contraction of the arterioles, and thereby raises the blood pressure. To some people digitalis in the form of tincture or infusion is an irritant poison; it causes severe pain in the stomach,

accompanied by vomiting and purging. By means of the hypodermic injection of digitalin, these unpleasant effects can be avoided.

Treatment.—Aconitine.—If seen early, use of stomach pump, emetics, tannic acid, or vegetable infusions, with or without potassium iodide. Cardiac and alcoholic stimulants, friction of the skin, hypodermic injections of digitalin, and maintenance of the body temperature by external heat.

Cocaine.—In addition to the treatment laid down generally, we must combat depression by alcoholic stimulants, or by ammonia administered by the mouth, rectum, or hypodermically. Inhalations of nitrite of amyl, or of oxygen, must be given to relieve asphyxia; and should the breathing cease, artificial respiration or the application of electricity must be resorted to.

Morphine.—It is advisable to wash out the stomach, so as to remove any of the drug that has not been absorbed, even though emetics may previously have been administered and vomiting occurred. The addition of permanganate of potassium to the water for lavage (1 per cent. solution), has proved extremely successful. After the viscus is thoroughly cleared out, hot strong coffee may be carried in by the stomach-pump, and allowed to remain therein. To prevent sleep, the patient must be kept walking about, care being taken not to push muscular exertion to the extent of exhaustion, nor, on the other hand, too readily to give way to the imploring requests of the patient to be allowed to sleep. The breathing must be watched, and increasing feebleness met by artificial respiration, which may have to be persisted in for a considerable time, two to three hours or even longer. Morphine and opium particularly paralyse the activity of the respiratory centre. Its automatism is destroyed. The centre will respond, however, to the influence of artificial respiration. If this can be maintained for some hours, breathing again becomes automatic. Stimulants, alcoholic and ethereal, will be required, if there is flagging of the circulation; also the subcutaneous injection of atropine, $\frac{1}{60}$ to $\frac{1}{30}$ gr., which may be repeated thrice within the hour if necessary. Inhalation of oxygen and the application of electricity may be employed; but where life is threatened, there is nothing that is more likely to prove successful in averting death than artificial respiration, kept up by relays of assistants, for several hours, until the poison is to some extent excreted from the system. The catheter should be passed from time to time to prevent reabsorption. Renewed lavage of the stomach may be necessary, as by its mucous membrane the poison is largely eliminated from the blood, only, however, to be reabsorbed if the contents are not removed.

Strychnine.—If the drug has been swallowed, give emetics, or use the stomach-pump. Should convulsions, however, have developed, it may be necessary to administer chloroform, so as to allow of the stomach being washed out. Chloral may be administered. Asphyxia may be warded off by inhalations of oxygen. Absolute quietude in the room and house generally is essential; and the patient should be touched and handled as little as possible.

Digitalin.—When an overdose has been taken, in addition to the general lines of treatment already mentioned, the administration of stimulants is called for to counteract the depression; also warmth to the surface, rest in the recumbent position, and opium to relieve pain. A hypodermic injection of strychnine or of some stimulant may be administered, if the heart is failing.

POISONING BY GRAIN, ERGOTISM, AND PELLAGRA.

Etiology.—Ergot is a drug of vegetable origin, belonging to the class known as oxytoxics, *i.e.*, remedies which excite uterine action during or after parturition. It is a blackish body—1 in. in length—grooved on one side and generally curved. On microscopical examination, ergot is found to be composed of cells rich in oily matter, but wanting in starch. The origin of the word ergot is doubtful. It was originally written "argot." In the French dictionary ergot is translated, " the spur of a cock or the claw of a dog." More than likely it is from its resemblance to a cockspur that the ergot of rye received its name. Its true nature was long unknown, but Tulasne clearly demonstrated its relationship to vegetable fungi, and to his work it may be said little has since been added regarding the botany of ergot. There are two stages in the life of a fungus. In the first a fungus exists as a mycelium or a filamentous structure, and in the second as a thallus or ordinary fungus, which perishes shortly after having brought to maturity its reproductive bodies. Between these two stages in certain fungi there is an intermediate one, in which the plant exists as a sclerotium. The genus *Claviceps* comprises many fungi which develop in the pistils of the various species of the gramineæ or grasses. Each of the dark bodies familiarly known to us as ergot is the sclerotium of the *Claviceps purpurea*, which infests the grain of *Secale cereale*, or rye. In a spikelet of rye or wheat that is becoming infested with the fungus, a sticky, sweet, but malodorous exudation is observed trickling from one of the flowers. It contains sugar, and, like other products arising from the irritation of vegetable tissue by fungi, is known as " honey dew," a substance extremely attractive to ants and beetles, but avoided by bees. Once " honey dew " appears on rye, ergot is sure to follow, for shortly afterwards there is observed at the base of the pistil a flocculent mass of mycelial filaments, which in their growth invade all parts of the ovary and pistil, ultimately forming an irregular dark body, a sclerotium that finally develops into commercial ergot. Most of the ergot used in medicine comes from Russia and Spain. Ergot is itself liable to be invaded by an acarus; this insect may so destroy the whole of the interior that it leaves simply a shell filled with excrement. The ergot used in medicine is the blight that has developed upon rye, but this blight is found also upon wheat and other cultivated grains. The ergot of wheat differs from that of rye in being shorter and thicker, but it possesses almost equal medicinal properties. Ergot contains nearly 35 per cent. of oily matter, and an ammoniacal base known as trimethylamine. It is not definitely known upon what its activity depends. Ecboline, ergotinine, and ergotine are the alkaloids that have been obtained from it; in addition, there are ergotinic, sphacelinic, and sclerotinic acids. The watery extract, ergotine, contains in a condensed form the activities of the drug. Kobert, who has given considerable attention to this subject, is of opinion that sphacelinic acid and a substance he calls cornutin are the poisons present in ergot.

Pathology and symptoms.—Two varieties of ergotism have been described—the gangrenous and the spasmodic. The symptoms observed in the Paris epidemic of gangrenous ergotism in 1828 were itchiness of the skin, vomiting, giddiness, abortion amongst pregnant women, arrest of the mammary secretion of suckling women, pains in the limbs, diarrhœa, erythema of the skin, ecchymoses or bullæ, numbness and tingling of the extremities, succeeded by anæsthesia, paralysis, and gangrene, sometimes

dry at other times moist, which destroys the part affected. In *spasmodic* ergotism, the severer cases presented, in addition to many of the symptoms just enumerated, painful contractions of the limbs, passing into tetanus, and followed by opisthotonos. During the intervals of relaxation there were epileptic paroxysms, delirium, complete or incomplete blindness, and loss of consciousness. Many of these symptoms persisted, and left the individual either insane or idiotic for life. In ergotism the pathological changes are found principally in the blood vessels. Recklinghausen found hyaline thrombi in the arterioles and capillaries, the arterial walls thickened and undergoing hyaline degeneration. Thoma states that the gangrene of ergotism is preceded by sensory and vasomotor disturbance; hence the pallor of skin, succeeded by reddening; the presence of vesicles that become pustular; and, finally, gangrene of the extremities, owing to persistent contraction of the small arteries, a contraction attributed by some writers to the action of sphacelinic acid present in the ergot. Kobert is also of opinion that it is the sphacelinic acid in the ergot that causes gangrene. Grünfeld fed animals with the acid, and he found in cocks that the comb soon became gangrenous, that in hogs the ears became gangrenous and fell off, and that the skin of dogs and cats also became gangrenous. At the post-mortem examination of animals poisoned by ergot, Krysinski found the epithelial lining of the intestine necrotic in patches, with small hæmorrhages in the mesentery. The only changes observed in the central nervous system have been degenerations in the postero-lateral columns of the spinal cord. There are probably cerebral changes as well, for only thus can we explain the convulsions and the other phenomena observed in spasmodic ergotism, phenomena which Moxon thought resembled the paroxysms of tetany observed in this country. As in England there has been little of either epidemic or sporadic ergotism, we shall for a description of the ergot convulsion simply quote the words of Romberg: "The hands and feet are attacked by cramp of the flexor muscles; the fingers of both hands are bent like hooks, the thumbs being pushed under the fore and middle fingers in an oblique direction; the wrist is strongly curved inwards, so that the hands assume the shape of eagle's beaks; the toes are doubled under the sole of the foot."

Rayer, who witnessed the epidemic in Paris in 1828, described the disease as acrodynia. He considered that it closely resembled pellagra, and that it was due to unhealthy cereals and ergotised rye. Ehlers seeks to establish an identity between the local asphyxia observed in the extremities in Raynaud's disease, and the swelling, coldness, and blueness of ergotism. He quotes one of Raynaud's cases, where a young woman during labour received 23 grs. of ergot. Three days afterwards she suffered from irregularity of the heart, fainting, and purging. Within three months there developed cyanosis, and coldness of the extremities followed by gangrene. Obstetrical ergotism has followed even smaller doses. The drug when administered for a lengthened period has caused local conditions in the extremities, resembling those observed in Raynaud's disease, also degenerative changes in the myocardium. In my own practice I have observed such unpleasant symptoms as vertigo, general numbness, staggering gait, muscular paresis, and loss of speech, in women who had taken ergot to check metrorrhagia, symptoms which gradually disappeared on discontinuing the use of the drug. In addition to ergotism, poisoning by grain may occur when the corn is not properly washed or cleansed before being ground. Several of the foreign wheats which I have examined

during my official inspection of flour mills for the Home Office, were found to be very dirty, especially those from the River Plate and Persia, particularly the latter, which frequently contains manurial filth. Owing to the very effective methods of cleansing and washing wheat which we now possess, foreign wheat is thoroughly cleansed of all such impurities before it is ground into flour, so that there is no danger from this source. All sorts of weeds and seeds are frequently present with the wheat grains, such as cockle, rye-grass, and ergot. Lehmann found that bread baked from flour containing more than ½ per cent. of cockle was unsuited for human food, and that when ergot was present and exceeded ·2 per cent., that it might give rise to unpleasant symptoms.

Although scarcely regarded as a poison, since large doses may be required to produce symptoms, it is yet capable of causing salivation, vomiting, dilated pupils, hurried respiration, and quickened pulse, staggering gait, paraplegia, and sometimes convulsions and death. Man responds very unequally to poisonous doses of the drug. Under its influence pregnant women have aborted. In men and in non-pregnant women, in addition to the symptoms just mentioned, it has caused anæsthesia of the surface, coldness of the extremities, and paralysis of the special senses. Its action upon the uterus has been known to the European peasantry for more than two hundred years, yet it was only in the early part of this century that the drug was formally introduced into medicine by Dr. Stearns of New York. Ergot acts principally upon the nervous system, and especially upon the centres that regulate the circulation. Courhant in 1827 advanced the opinion that the drug caused spasm of blood vessels, and in 1870, Holmes demonstrated under the microscope, in the web of a frog poisoned by ergot, that both arteries and veins were much contracted, a fact confirmed by other experimenters and by the ophthalmoscopic examinations made by Nicol and Mossop, who observed very marked contraction of the retinal vessels in man after administering the medicine. The arterial pressure first falls, then rises, owing probably to stimulation of the vasomotor centre. When toxic doses are administered, the blood pressure falls, owing to paralysis of this centre. The intestinal musculature is contracted. The body temperature falls. The action of ergot medicinally is principally upon the womb and small blood vessels. It has little influence upon the unimpregnated uterus, and very little directly upon the uterine fibre itself. It is supposed to operate chiefly through the centres in the lower part of the spinal cord, whereby contraction of uterine muscular fibre is first induced, and then tetanus. Domestic cattle are said to be specially susceptible to ergot poisoning. Several epidemics of loss of calves by cows have been traced to eating ergotised grain, while guinea-pigs, rabbits, and cats are also known to have aborted.

Ill health, consequent upon the ingestion of bread made from blighted grain, has of late years been less observed than formerly, owing to improved methods of agriculture, and the more rapid international transit of farm produce. During the past centuries there have occurred several epidemics of gangrene due to this cause. Under the names of the "holy fire" of antiquity, erysipelas of Greek authors, and "St. Anthony's fire" of the Middle Ages, epidemics are described which are now considered to have been ergotism. For a recognition of ergotism and its cause we are indebted to Thuillier and Tessier. One of the earliest epidemics occurred in 857, and is mentioned in the annals of the convent of Xanthen on the Rhine. Nearly a hundred years after, a similar epidemic broke out in Paris. Subsequently Aquitania

was so severely scourged by ergotism that 40,000 people died from "an invisible fire, consuming the body and separating from the trunk the members that had been attacked." As the cause of the disease was unknown, it was regared as a "visitation." France experienced several epidemics from 1090 onwards. Frequent civil wars and Norman invasions had so transformed the north and central parts of France and destroyed the population, that the fields were no longer cultivated, and the result was starvation. Other countries were not spared. An epidemic at Lüneburg in Germany in 1581 caused 532 deaths. The epidemic broke out in Westphalia, where it was known as *spasmus pestilentialis*, and attributed to bad bread and improper nourishment. Thuillier, who was physician to the Duke of Sully, was an eyewitness of the epidemic as it ravaged Sologne. It was he and the Abbot Tessier who published the first scientific account of ergotism. The soil is described as having been wet; vegetable production scanty and diminutive on account of the barrenness of the ground and coldness; the people were much reduced in health, and became the subjects of intermittent fever. Thuillier maintained that ergotised rye was the cause of the epidemic, that the severity of the illness was proportional to the amount of poison taken, and that the malady was especially prone to appear during wet summers following cold winters. In order to convince others that ergot of rye caused gangrene, he administered the poisonous grain to several animals, which were killed by it, an experimental demonstration which was soon afterwards realised in nature by animals dying wholesale from eating poisoned grain. Bread made from diseased rye rendered those who ate it liable to gangrene. It was in Sologne that the spoiled grain was first called ergot. During 1716 gangrene appeared in the cantons of Lucerne, Berne, and Zurich, among people who had partaken largely of vitiated grain. Where only small quantities had been eaten, the illness was limited to a sense of weight in the head, numbness of the extremities, and a form of drunkenness, especially in those who had eaten their bread hot.

All the writers of last century agree as to the epidemics having principally attacked the poor, and that at the time the crops were scanty. The disease frequently appeared at the close of long wars and bad seasons. So great was the scarcity of grain then, that the peasantry were sometimes compelled to eat bread made of acorns, grape seeds, roots of ferns, and other herbs, cooked without salt, or any kind of seasoning. As late as the early part of last century we read of an epidemic in Silesia, treated empirically by means of lycopodium seeds and human blood freshly drawn. The country lying between Moscow and the Volga was also affected, and with such severity that in the neighbourhood of Nijni it is estimated that 20,000 people died. Civilisation and improved methods of agriculture have gradually driven ergotism further and further east, to countries where localities are insalubrious for the drying and winnowing of grain. Ergotism becomes gradually unknown wherever grain is properly dried. As there have always been isolated and apparently sporadic cases in the intervals between epidemics, Ehlers is of opinion that such diseases as acrodynia, Raynaud's disease, and erythromelalgia are forms of mild ergotism.

Rye bread still forms the staple article of food of the lower classes in many parts of Europe, particularly in Russia. At the end of the harvest the ergotised grain is not always sufficiently carefully separated from that which is healthy, and the result is that the bread of the peasantry nearly always contains a small quantity of the mould. After a wet and cold

summer the rye is frequently much ergotised, and it is then that ergotism appears, but how far it is due to any specific action of ergot it is difficult to say. Trousseau and Pidoux regarded the epidemics as due to disordered blood conditions, consequent upon improper and insufficient food, and attributed them to general poverty and starvation, for if ergot is administered to people living under normal conditions it does not cause gangrene.

In Lombardy and the adjacent countries there occasionally prevails a disease known as *pellagra*, from *pelle* skin, and *agro* rough, because the skin becomes inflamed or rough. Fifty-six thousand cases are reputed to have occurred in Lombardy alone in 1881. The patients presented symptoms connected with the skin, digestive organs, and nervous system. At first the skin was red, painful, and swollen. This was followed by loss of appetite, distaste for food, and by diarrhœa; and subsequently, in the severe cases, by extreme prostration, delirium, and paraplegia. Many of the patients died, and at the autopsy numerous small ulcers were noticed on the skin, and in the intestines. On microscopial examination, degenerative changes were found in the spinal cord. Paltauf and Heider considered the illness to be due to the ingestion of corn meal, infected by the *B. maidis cuboni* and the *B. mesentericus fuscus.* Vaughan believes that the germs which cause the disease produce ptomaines, which alike in their chemical and physiological reactions resemble strychnine, and cause tetanic spasms in animals. In 1871, Lombroso demonstrated that from mouldy corn meal an extract could be obtained which produced tetanic convulsions. He named it *pellagrocine*, a complex body composed of several ptomaines, some of which produce narcosis and paralysis, while others induce cardiac and respiratory failure. Clifford Allbutt, in his account of pellagra, shows that, like ergotism, it is a disease of the poor, and due to bad maize. It is a form of ptomaine poisoning, which, in addition to causing erythema and gangrene of the skin, induces a lesion in the lateral columns of the spinal cord, hence the paralysis met with during life.

Diagnosis and prognosis.—The diagnosis of epidemic ergotism rests upon the history of a cold, wet summer, blighted grain, and the prevalence of the symptoms of the disease chiefly amongst the poor, who are known to have been eating bread made from diseased rye or wheat; of sporadic ergotism, upon the presence of the symptoms already detailed, along with such facts as may be explained by arterial ischæmia.

When ergotism attacks elderly people the prognosis is naturally graver, on account of the state of the heart and arteries incidental to age.

Treatment.—When the disease is epidemic, the ravages of ergotism should be met by improving the character of the food, by destroying all bread that has been made out of blighted grain, and substituting for it bread made from healthy cereals. General and local warmth, carefully applied, if the extremities are numb or commencing to be gangrenous; the administration of stimulants, and medicine to allay gastro-intestinal irritation, if present. Contracted limbs should be treated by massage and electricity. Amputation of the gangrenous extremity must be resorted to when necessary.

LATHYRISM.

In addition to ergotism and pellagra, consequent upon eating diseased grain, Kobert and Cantani have drawn attention to a series of symptoms caused by eating food made from the seeds of the common vetch or chick-pea. Like ergotism, the disease has generally appeared after a failure of the wheat crop. This was the case at Allahabad, as reported by Irving. Lathyrism has been mostly observed among the peasantry of Spain, France, and Italy, and in certain parts of India. It assumes the epidemic form, and affects principally males, in whom it causes a transverse myelitis attended by sensory and motor paraplegia. Occasionally the paralytic symptoms disappear, but there remains a degree of spastic tabes with heightened tendon reflexes. Lathyrism develops quickly, the earliest symptoms being stiffness of the limbs, pain in the back, formication, altered sensation, and spastic gait. Men and animals, but particularly horses, are affected by it. Hogs are said to be quickly killed by eating vetch, and horses suffer from paralysis of the recurrent laryngeal nerve requiring tracheotomy. The muscles in man and animals have been found to have undergone fatty degeneration, and the multipolar cells in the anterior horns of grey matter in the spinal cord to have become diminished in number and atrophied.

It is not exactly known upon what particular substance in the vetch the poisoning depends

THOMAS OLIVER.

SECTION IV.

ALIMENTARY SYSTEM.

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DISEASES OF THE MOUTH.

THE mouth is subject to many diseases, several of which are due to local inflammation, while others are manifestations of a general disease, such as syphilis. Some of the local infections, for example, diphtheria, scarlet fever, measles, are discussed elsewhere.

The local affections which occur in the mouth may be due to local causes, with a predisposition, in some cases, due to the general condition of the body. Numerous bacteria are found in the mouth. Some of these are taken in with the food and air, and increase in the mouth and throat, their growth being aided by the presence of dirty or decayed teeth. Through the mouth also comes sputum from the lungs, and in this way a patient with pulmonary tuberculosis may infect the mucous membrane, causing a tuberculous ulcer. Over thirty varieties of bacteria have been found in the mouth by Miller and others. Many of these are pathogenic—some are unnamed. The pathogenic micro-organisms are chiefly the *Staphylococcus pyogenes aureus* and *albus*, and the *Streptococcus pyogenes*, as well as the micrococcus of sputum septicæmia (*Diplococcus pneumoniæ*), and the *Micrococcus tetragenus*. The pus micro-organisms are not constantly found in the mouth, but inasmuch as they are present in the air their occurrence in the mouth is always a possibility. One fungus, the oïdium albicans (*Saccharomyces mycoderma*), is found.

Animal parasites also occur in the mouth and tongue, such as hydatids, which are rare, the guinea worm, not found in this country, and the trichina spiralis.

STOMATITIS.

Stomatitis is an inflammation of the mouth produced by the growth of bacteria and by various irritants, mechanical and chemical, such as boiling water and corrosive substances, and mercury administered internally. It occurs also more especially in children, in acute specific diseases, like measles, diphtheria, acute bronchitis, and scurvy ; is no doubt due, in these conditions, to a predisposition to infection, induced by a lowering of the resistance of the body by the primary disease.

CATARRHAL STOMATITIS.

Stomatitis is sometimes chiefly a catarrhal condition. There is generally an increased secretion of mucus by the glands, with diffuse areas of redness and some swelling of the mucous membrane. This is frequently accompanied by salivation, and the lips, as well as the mucous membrane inside the mouth, are affected. In mercurial stomatitis there is profuse salivation, with swelling and sponginess of the gums, which readily bleed, and may ulcerate, and there is intense fœtor of the breath.

In ulcerative stomatitis, which is usually observed in children, there are numerous superficial ulcers of the mucous membrane of the mouth and lips, surrounded by a zone of congestion, and accompanied by a thickening of the mucous membrane generally. The mouth is open, and dribbles with a discharge (which is partly purulent, partly mucoid) as well as with saliva. A dirty feeding-bottle is a frequent cause of the disease in infants. In some cases the stomatitis is more localised, and arises definitely near the tartar of the teeth. This form consists in a slowly spreading ulceration of the mucous membrane, which may pass on to the lips, and lead to more or less extensive but superficial destruction. Such cases occur chiefly in low conditions of health, such as pulmonary consumption, and in this case the smooth ulcer may become infected by the sputum, and a tuberculous ulcer develop. The treatment in such a condition is the application of strong antiseptics, followed by boric acid lotion, and when it becomes tuberculous, by a scraping of the ulcer.

Treatment.—Acute stomatitis is readily treated. If it be due to mercury, the administration of the drug must be stopped. In all cases the other treatment is similar. The mouth must be kept constantly washed out with an antiseptic lotion, such as warm boric acid lotion, or a dilute alkaline lotion—bicarbonate of sodium (5 grs. to the ounce). After washing the ulcer, it must be dried by a piece of clean linen. The parts which are most ulcerated may be treated by a careful application of a solution of mercuric chloride (1 in 2000), the ulcer being dried after the application. Glycerin and borax is also sometimes useful. In some cases, especially in the ulcerative stomatitis of children, chlorate of potash is a specific; the mouth being washed with a solution (10 grs. to the ounce), and the drug administered internally in doses of 1 to 5 grs. It must be remembered that chlorate of potash produces poisonous symptoms sometimes, and may lead to hæmoglobinuria.

APHTHOUS STOMATITIS

Thrush is an inflammatory condition of the mouth, shown by local superficial erosions, and produced by a fungus called the oïdium albicans. In some cases it seems certain that the infective agent is not the oïdium, but various forms of bacteria. The oïdium is seen in the form of hyphæ and spores, mixed with the epithelium of the mouth and the tongue. It may be demonstrated by soaking the scrapings of the aphthous ulcer in liquor potassæ.

The aphthous ulcer is small, one-eighth to one-fourth of an inch in diameter; it is surrounded by a zone of congestion, and covered by a white or whitish yellow layer, containing the fungus with the epithelium. The edges are but slightly raised, and the base, on removing the covering, is

reddened. The ulcers are painful and tender, and lead sometimes to a difficulty in chewing the food.

Thrush is most common in children, but it is observed in adults, in association with digestive disturbances, and in the later stages of wasting diseases. In children it is constantly associated with gastro-intestinal disturbances. Its appearance is frequently ushered in by vomiting and diarrhœa, and by some degree of fever, due to the intestinal disturbance. It may be associated, in these cases, with ulceration of the anus or inter-trigo; but when there is ulceration of the anus, these cases are usually congenital syphilis.

Treatment. — The treatment of thrush is that of the intestinal disturbance. The administration of alkalies or bismuth, or mercury and chalk, and the local application to the ulcer of glycerin and borax, or nitrate of silver solution (10 grs. to the ounce), or solution of corrosive sublimate (1 in 2000), or of glycerin of carbolic acid (1 in 20).

GUM-BOIL.

This is the result of an inflammatory condition of the gums, secondary to caries, such as periostitis of the root or abscess. Not much need be said of this condition, inasmuch as its consideration, as well as that of its results, namely, alveolar abscess, belongs to the domain of surgery. Alveolar abscess may open, according to its situation. on to the cheek, into the mouth, or into the antrum. The treatment is surgical.

Of non-inflammatory diseases of the mouth may be mentioned ranula, a cyst which is formed at one side of the frenum, which is painless in its growth, and does not develop to a size greater than that of an almond. It is probably either a retention cyst of a buccal gland, or a cyst of a salivary duct. Epulis, which is a fibroma of the gum, is not infrequently met with. The treatment of these conditions is surgical. Cancrum oris is described amongst the general diseases.

SIDNEY MARTIN.

DISEASES OF THE TONGUE.

THE conditions of the tongue to be considered are—(1) affections in which there is an actually diseased condition present in the tongue, and (2) changes in the tongue, showing indications or signs of disease. The tongue itself is subject to ulcerations, which are of various kinds, either simple or specific (syphilitic, tuberculous, or cancerous).

Chronic inflammation may be superficial or lead to the formation of chronic abscess, or, as in other cases, to a thickening of the surface of the tongue. The tongue is subject also to hypertrophy and to atrophy, secondary to conditions of the central nervous system, and to new growths, either simple or malignant, as well as to dermoid cysts.

ULCERATION.

The tongue is subject to various forms of ulceration—traumatic, dyspeptic, aphthous, syphilitic, tuberculous, cancerous.

Traumatic Ulceration of the Tongue

usually results from a decayed tooth, so that the ulcer most frequently is at the outside of the tongue, about the middle, or towards the anterior part. It is first shown as a soreness at the side of the tongue, and on examination an ulcer is found, not, as a rule, large in extent, surrounded by some thickening and congestion. Traumatic ulcers may also be due to injury, following a bite of the tongue such as frequently occurs in an epileptic fit.

The treatment of traumatic ulcer of the tongue is by removing the cause, for example, a jagged tooth, and by applying a mild antiseptic wash to the mouth. When the ulcer does not heal readily, the application of nitrate of silver is of great service.

Dyspeptic Ulceration

or ulceration in association with diseases of the stomach, is not common on the dorsum of the tongue; it is more frequently observed on the under surface, and on the gums and cheek. It is a superficial ulceration, which tends to spread somewhat, the edges being very slightly thickened, and the base even. Such ulcers are most common in cases of diminished vitality of the system, associated with gastric disturbances. They usually heal when the patient improves in general health, and are best treated by means of the constant application of boric acid solution, and the occasional application of glycerin of carbolic acid (1 in 20) or of tincture of benzoin.

Syphilitic Ulceration

is of frequent occurrence in the tongue. It usually occurs in the initial stages of the disorder, and is seen as an irregular ulceration on the sides, and at the top of the tongue; with a whitish base and some thickening around. As in other syphilitic ulcerations of the mucous membrane, there is frequently cicatrisation at one part and ulceration at another. Mucous tubercles may also be present. Sometimes the ulceration spreads over the dorsum of the tongue, producing eventually much scarring and destruction of the epithelium. The surface of the tongue may in these cases be very irregular, with whitish patches of fibroid tissue in parts, and red and glazed, or even with a bluish surface at other parts. Such a condition cannot be mistaken for anything but syphilis.

Gumma of the tongue occurs in a later stage of the disease, as a mass in its substance. It is usually at the posterior part. The swelling is painless, and tends to ulcerate, the discharge being sanious.

The treatment of syphilitic disease of the tongue is that of the general disease. The local treatment consists in the application of nitrate of silver in a solid form to the ulcer, and of a wash of mercuric chloride (1 in 5000), or of mercuric bicyanide (2 grs. to the ounce).

Tuberculosis of the Tongue

as a primary disease, is practically unknown. It is observed in the later stages of pulmonary tuberculosis, and is, no doubt, due to the infection of a crack in the tongue by the sputum as it passes through the mouth. The ulcer which is eventually formed is irregular, with an uneven base, covered by somewhat cheesy matter, and with whitish thickened edges.

From the appearance it is impossible to distinguish it from gumma. The diagnosis is made from its association with pulmonary tuberculosis, and from the fact that it does not yield to treatment by mercury. It may be treated by the application of cocaine and scraping, or by the application of mercuric chloride in solution, and the mouth washed with a solution of bicarbonate of soda and glycerin, or with a permanganate of potash solution.

CANCEROUS ULCERATION.

Cancer of the tongue occurs in the form of squamous epithelioma. It originates at the base of the tongue, usually at the middle or at one or other side, and is characterised by a gradual infiltration and thickening of the tongue itself, and of the surrounding parts. Subsequently it ulcerates, an irregular ulcer with an irregular base being formed, giving forth a sanious discharge, which frequently becomes fœtid. In its early stage it is difficult or impossible to distinguish from gumma; but it is not diminished by the use of mercury, and tends rapidly to infiltration, as well as to an affection of the glands below the jaw. The treatment of cancer of the tongue is surgical.

TUMOURS.

The other forms of tumour, besides cancer, that occur in the tongue are papillomata, which occur in the form of warts; fatty, fibroid, cartilaginous, and bony tumours; cavernous angioma or nævus, as well as mucoid cyst, also occurs. But little need be said of these growths. They are all slowly growing, producing but little or no pain; the warts and fibrous tumours project from the surface, while the others are in the substance of the tongue. The mucoid cysts are usually found at the base of the tongue, and project on the surface. They may be confounded with solid tumours, or with chronic abscess; the diagnosis is made when they are opened.

INFLAMMATION.

The whole of the tongue may become inflamed, as when a powerful irritant is applied to it; for example, in the case of swallowing corrosive poisons, of the sting of a wasp, or of a septic wound to the tongue. Some cases of macroglossia are of this nature. The tongue is greatly enlarged, painful and tender, and swallowing becomes impossible. The lips are also enlarged, and the glands below the jaw become affected. The treatment of glossitis is surgical, and consists in the making of incisions in the tongue. Inflammation of the tongue may, however, be more limited, so that only a superficial glossitis results. The cause is still an irritant, such as scalding or a corrosive poison, or the effects of the administration of mercury. The dorsum is the part chiefly affected, and is swollen, reddened, and smooth, the epithelium being more or less cast off. By the use of warm mouth washes the inflammation subsides.

Chronic abscess of the tongue is a rare condition, and usually forms a swelling just in front of the circumvallate papillæ. It is of slow formation, and has thickened edges, and sometimes fluctuates. The condition is treated surgically.

What may be considered as a chronic inflammation of the tongue occurs in the form of leucoma and ichthyosis. The condition is usually seen in middle age, and is no doubt due to irritation of one form or another. In leucoma there are white patches on the dorsum of the tongue, due to a thickening of the mucous membrane, but there is no roughness of the surface.

In ichthyosis, also termed psoriasis or keratosis, but better known as leucoplakia buccalis, the dorsum is usually affected, and there is great hypertrophy of the papillæ, giving the appearance either of a shaggy coat or of the rough skin of a fish. In some of these cases there is a history of syphilis, with other cases epithelioma is associated.

ATROPHY.

Atrophy of the tongue occurs as the result of lesions of the central nervous system, or of the hypoglossal nerve. In the latter case it is almost always unilateral; in the former case it may be unilateral or bilateral. The diseases in which it is usually found are glosso-labio-laryngeal palsy, in which the nucleus of the hypoglossal nerve is affected, disseminated sclerosis or tabes, which spreads up to the medulla. Paralysis in these cases precedes, or is coincident with, the atrophy, and the movements of the tongue become greatly limited.

HYPERTROPHY.

Macroglossia occurs as a congenital defect, and is associated with congenital mental deficiency. It is frequently associated with a thickness of the lips (macrocheilia), so that the patient usually has protruding lips, with a large tongue between, and an idiotic expression. Saliva dribbles from the mouth, and ulceration of the tongue and lips frequently occurs, with fœtor of the breath. This condition is to be distinguished from the enlarged tongue, the result of inflammation.

THE TONGUE AS AN INDEX OF DISEASE.

Besides the local diseases to which the tongue is subject, and the diseases which are due to local conditions, the tongue may be affected by general diseases of the body. The conditions now to be discussed are four in number, namely, the furring of the tongue, dryness of the tongue, enlargement of the papillæ, and flabbiness of the tongue.

Furring of the tongue occurs in many different conditions. The fur may be distributed all over the tongue, or only at the back, and consists partly of epithelial scales and partly of micro-organisms. When a furred tongue cleans, the fur disappears first from the tip and edges, and last of all from the posterior part. Sometimes it cleans uniformly, at other times in patches or flakes; the fur originally may have been in patches, giving rise to what has been called the "stippled" tongue (Dickinson). The furred tongue may be associated with enlargement of the fungiform papillæ, and this enlargement of the papillæ may persist after the tongue is clean.

The rapid cleaning of the tongue, with denudation, in part, of the superficial epithelium, as well as the continued enlargement of the papillæ, gives rise to the red and raw or glazed tongue; whereas the enlargement of papillæ, with whitish patches in between (usually at the tip), gives rise

to the "strawberry" tongue. The tongue becomes furred in local diseases, such as inflammation of the tonsils, and of the mouth generally. The side on which the inflammation is most intense is more furred than the other; thus, if one tonsil is more inflamed than the other, that side of the tongue is most furred; similarly, where a tooth produces inflammation of the tongue, that side becomes furred. The tongue becomes also furred from general disease, the chief of which is the condition of pyrexia. In all acute fevers this is the case, such as typhoid, typhus, rheumatic, and scarlet fevers, variola, and many others. In nervous diseases of acute onset the tongue also becomes furred, such as in the epileptic state, in apoplexy, and in neuralgia, where the tongue is not infrequently furred unilaterally, that is, on the side of the pain. In diseases of the stomach the tongue is furred in acute attacks of gastric irritation and gastric catarrh. In ulcer of the stomach and in gastric insufficiency the tongue is not usually furred, and in cancer the furring is variable. In acute liver conditions the tongue is also furred, but in these cases furring is as frequently to be ascribed to the stomach as the liver.

The broad, pale, flabby tongue is the tongue of anæmia, of Bright's disease, and of wasting diseases. It is no doubt the direct result of the anæmia produced by these conditions. In Bright's disease the tongue may also be œdematous.

The dry tongue is due directly to diminished secretion of saliva, as well as to the fact of sleeping with the mouth open. A condition of high fever leads to dryness of the tongue, as there is a diminished secretion of saliva. In a similar manner, an increased excretion of water from the body leads to dry tongue, as in polyuria, excessive sweating, and profuse diarrhœa. To this cause must be ascribed the dry tongue which occurs not infrequently in cases of dilatation of the stomach. Dry tongue is also observed in cases of bodily prostration, and is the characteristic tongue of nervous people. What may be called "a nervous tongue" is pale, usually dry, and at other times covered with a thin froth. The dry tongue in pyrexia is a sign sometimes of high temperature, sometimes of great bodily prostration, and is a symptom which must always be looked upon as somewhat serious. One of the signs of improvement in the febrile patient is when the dry tongue becomes moist, as it does in the period of defervescence and during the administration of alcohol. One of the signs of alcohol doing good in fevers is when the dry tongue becomes moist under its influence. The dry tongue in diabetes becomes moist again when the amount of sugar in the urine greatly diminishes. Dry tongue and xerostomia in gastric irritation disappear when the stomach condition is relieved.

Pityriasis linguæ (annulus migrans, lichenoid) is a curious condition of the tongue, sometimes confined to one side, sometimes present all over the dorsum and the under surface of the tongue. It occurs in the form of circles or curves, which are whitish in appearance, and due to the enlargement and the cornification of the papillæ. The centre of the curve is bare, and the papillæ, to some extent, have here lost their epithelium; the tissue below is infiltrated with leucocytes. It is evanescent, the eruption coming and going without obvious cause. Its causation is unknown, no definite parasite having been found associated with it. Treatment, whether antiseptic or otherwise, is of no avail. It occurs both in children and adults, perhaps more frequently in the former; it has been observed in children who have but slight ailments, but it may be associated with some severe and fatal disease.   SIDNEY MARTIN.

DISEASES OF THE SALIVARY GLANDS.

THE secretion of the three pairs of salivary glands is necessary for the moistening of the food and for the initial digestion of starch, so that changes in the secretion in disease are of some importance.

FUNCTIONAL DISORDERS.

In many people the diastatic action of the saliva is from time to time very deficient; the secretion may be either diminished or increased in disease. When diminished, it produces a condition which is called xero-stomia, or dry mouth; when increased, it produces salivation, saliva filling the mouth and running from the corners of the mouth. Diminution of the secretion occurs in inflammatory conditions of the mouth (ptyalism), in fever, in belladonna and stramonium poisoning, and in conditions in which there is increased excretion of water from the body, such as in profuse perspiration, in diabetes, in polyuria, and in prolonged diarrhœa. The most marked cases of xerostomia, as well as the most prolonged, are observed in certain conditions of the stomach, such as those associated with a hypersecretion of hydrochloric acid. The treatment of xerostomia is directed to the relief of the local condition by the use of glycerin and borax, or by a continuous washing out of the mouth with tepid water without swallowing it. In cases where it is due to diabetes or a stomach condition, it is relieved when the amount of sugar diminishes in the urine, or when the stomach condition is improved. Increased secretion of saliva may occur, either from the reflex or direct effect on the salivary glands which is produced by certain drugs, such as mercury, iodine, tobacco, and pilocarpine. It also is produced in the early stages of local inflammatory conditions of the mouth, in excessive cough due to bronchitis; and it has been observed also as the result of emotions and pain, and in pregnancy and insanity. The treatment of ptyalism or salivation is in some cases possible, in others futile; thus, in salivation due to mercury, pilocarpine, or iodine, the condition ceases soon after the cessation of the drug. In that due to other conditions, small doses of belladonna may be employed (10 minims of the tincture three times a day), or small doses of pilocarpine may be administered.

ORGANIC DISEASES.

The diseases to which the salivary glands are subject are mumps, inflammation, new growth, calculus, and fistula of the duct. Inflammation is usually observed in the parotid gland (parotitis). It is a manifestation of pyæmia or septicæmia of whatever origin, and is frequently a valuable sign of such condition. It is a diffuse inflammation of the gland, which frequently ends in suppuration, either in one abscess, or in multiple abscesses distributed through the gland tissue. It is shown by a swelling in front of and below the ear, with a diffuse swelling of the cellular tissue around. The swelling is very painful and extremely tender, and its appearance may be ushered in by a rigor, and an increase of the fever caused by the primary disease.

Salivary calculi are like those which are formed sometimes in the

pancreas. They are present in the ducts of the gland, and are composed of carbonate and phosphate of lime. Fistula of the duct occurs sometimes as the result of a calculus, but more frequently as the result of inflammation of the cheek, whereby the duct is opened to the exterior.

The new growths which occur, chiefly in the parotid gland, are fibroma, chondroma, and malignant tumours. Chondroma forms a hard, slowly growing tumour, unilateral, and extending from below the lobe of the ear upwards in front to the ear, along the cheek. A malignant tumour has a similar position; it grows more rapidly, is softer, and infiltrates the surrounding tissues, as well as affects the neighbouring lymphatic glands.

<div align="right">SIDNEY MARTIN.</div>

DISEASES OF THE FAUCES AND TONSILS.

THE tonsils are affected by various diseases, some of which are due to a definite infection by micro-organisms; others are manifestations of a general disease; others, again, are local non-infective diseases. Thus the tonsils may be involved in the eruptions of varicella, variola, and herpes, and are the seat of inflammation in scarlet fever, measles, and certain other diseases to be discussed under "acute tonsillitis." They are also implicated in secondary syphilis, and a gumma may be present in the later stages; it is rarely the seat of tuberculous infection. Diphtheritic infection is discussed elsewhere. The rashes of varicella and variola, which occur in the fauces and tonsil, do not differ from the rashes of the skin, and need not be further described. The same may be said of herpes. In syphilis condylomata occur, which are more or less transparent projections associated with serpiginous ulceration. There is as well a diffused congestion of the parts, and the distribution of the condylomata is very irregular.

Tuberculous ulceration of the tonsil is very rare, and is usually associated with a similar ulceration of the pharynx. The ulcer has thickened edges and an irregular base, and is covered by white or whitish yellow patches, containing tubercle bacilli. The diagnosis is made from the great chronicity of the ulceration, and by the fact of its association with tuberculosis of the lungs. It never occurs as a primary disease, and is only observed in the later stages of pulmonary tuberculosis.

Malignant disease of the tonsil, whether sarcoma, lymphosarcoma, or epithelioma, is characterised by the same appearances remarked on in malignant disease elsewhere. Thus there is great enlargement of the parts, the disease being at first always unilateral, and extension of the growth across the soft palate, and to the cheek; while the glands below the jaw become enlarged, the enlargement being progressive, and leading, not infrequently, to adhesion to the skin, and subsequent ulceration. Ulceration of the growth on the tonsil is an occurrence leading to a very foetid discharge. The course of the disease is progressively downwards, unless a radical operation for its cure has been performed in the early stage.

The diseases which are to be more fully discussed in this place, are those which are the result of inflammation, whether acute or chronic, namely, acute tonsillitis, follicular tonsillitis, and chronic tonsillitis or hypertrophy.

ACUTE TONSILLITIS.

This is an acute parenchymatous inflammation of the tonsils produced by micro-organisms. The micro-organisms which have been found are either streptococci or staphylococci. Sometimes the streptococcus is found by itself, more commonly it is mixed with the staphylococcus. There may be other micro-organisms which produce inflammation of the tonsils, such, for example, as the pneumococcus.

Etiology.—Acute tonsillitis is frequently a primary disease, being due to direct exposure to infection. Of such a nature is the tonsillitis which follows on breathing emanations from drains, or that which occurs in hospitals and other public buildings, where there are large numbers of people housed with deficient ventilation and accumulation of dust. The infection is either associated with a low condition of vitality of the patient, or there may be a diminished local resistance, as when acute tonsillitis supervenes on chronic. It is a disease usually occurring in young adults, whether male or female, and is most frequent in children. Acute tonsillitis is associated with other diseases, the most common of which, perhaps, is rheumatic fever. Infection of the tonsils by bacteria also supervenes in scarlet fever, in diphtheria, in measles, and sometimes in whooping-cough, and even in rheumatic fever. Cultivations made from the throat, show that the condition is one due to direct infection by micrococci.

Symptoms.—Acute tonsillitis is sudden in its onset, being associated at first with a tickling in the throat and a sense of heat, and perhaps of dryness. The patient rapidly becomes febrile, the temperature rising to 104° and 105°; the fever being associated with malaise and bodily and mental depression. Headache, frontal in character, is common, and the patient takes to his bed. On examination, the throat may be found in varying conditions; the tonsils may be enlarged, but chiefly congested, as are the fauces and soft palate. The colour varies from reddish to purplish red, and the surface of the tonsils is frequently covered by a thin exudation, dirty yellow in colour, which consists partly of mucus, and partly of albuminous secretion, containing large numbers of micro-organisms. The glands below the jaw are enlarged, and surrounded by a diffuse swelling, which is tender on pressure. There is at this time great difficulty and pain in swallowing; the tongue is thickly covered with a yellow fur, and the breath becomes foul. Constipation is present, and the urine is diminished in quantity and loaded with urates. In some cases the tonsils do not present the appearances described above, inasmuch as there is more exudation on the surface. This exudation may be patchy in nature, and may form an imperfect membrane, which is, as a rule, readily removed by means of a brush dipped into a solution of nitrate of silver (10 grs. to the ounce).

From this point the course of the disease varies somewhat. The duration of the acute symptoms, if the treatment carried out is effective, is from four to five days, and the patient is usually well again in a fortnight. In some cases, however, suppuration occurs, and an abscess is formed in the tonsil. An abscess may be suspected if the fever keeps up, and if the swelling is very great, so great that the patient can hardly open his mouth; on examination with the finger, the tonsil on one or other side is found soft and fluctuating. The abscess sometimes ruptures spontaneously into the mouth, and in rare cases may lead to profuse hæmorrhage. Abscess of the glands of the neck also occurs.

Diagnosis.—The diagnosis of acute tonsillitis is to be made chiefly from diphtheria. The disease also may be distinguished to some extent clinically from cases of follicular tonsillitis.

In acute tonsillitis the infective agent may be of different degrees of virulence; infection by the streptococcus being more virulent than that by the staphylococcus, and the micro-organisms may form a membrane to some extent resembling that present in diphtheria. On the other hand, although the formation of membrane is the rule in diphtheria, it may be absent in a mild case, congestion or enlargement of the tonsils or fauces alone being present. These facts, together with the necessity in treatment of cases of diphtheria for the injection of antitoxic serum, render the diagnosis between simple tonsillitis and diphtheria a very important one. It is in many cases impossible, when the patient is first seen, to decide whether some cases are really diphtheria or not. Such cases are better distinguished as doubtful ones, and by some are erroneously called "diphtheritic throat," meaning thereby a throat like that of diphtheria, but not actual diphtheria. This nomenclature is very misleading, inasmuch as it leads to the non-employment of the curative agent (antitoxic serum) in a certain number of cases of diphtheria, which may be fatal.

A large proportion of these doubtful cases is readily diagnosed by means of a cultivation made from the throat on the surface of blood serum. In from eighteen to twenty hours, when the growth which occurs on the surface of the blood serum shows colonies of the *Bacillus diphtheriæ*, in the case of diphtheria, it may show only colonies of cocci if the case is one of simple tonsillitis. There are cases of real diphtheria, however, in which one, two, or even three cultivations from the throat show no definite diphtheritic bacilli; but these have to be classed as doubtful cases from an examination of the throat, and are to be considered clinically as diphtheria, and treated as such. Otherwise the diagnosis of acute tonsillitis gives rise to no difficulty. The knee-jerks are not exaggerated or absent, as in many cases of acute diphtheria, although the general bodily depression may be great, and albumin or even blood may be present in the urine.

Treatment.—In the early stage, when the patient is seen with a very furred tongue, with headache and high fever, the treatment is best commenced by the administration of a mercurial purgative, such as 3 or 5 grs. of calomel, followed after several hours by a dose of saline. This may be repeated on the following day, if necessary, and in all cases it is essential to keep the bowels well open. Other treatment is directed to the relief of the general symptoms; thus, in some cases continuous treatment with small doses of mercury and chalk is highly beneficial; in others, again, with high fever, the administration of small doses of aconite is useful, namely, 1 or 2 minims of the tincture every three hours, and then every hour for twelve hours. Larger doses of tincture of aconite are frequently given, but it must be remembered that aconite has a powerful depressing action on the heart. Salicylate of sodium, in 10- to 15-gr. doses, given every three hours, is frequently beneficial in relieving the general symptoms of the disease, and it has been stated by some to even cut short its course. It may be combined with ammonium chloride in 5-gr. doses. Guaiacum, in the form of ammoniated tincture, 1- to 2-drm. doses every three hours, is frequently useful in acute tonsillitis. It may be given with an alkali, such as bicarbonate of sodium, but it is apt to produce diarrhœa, and when this occurs its administration must be temporarily stopped. Tincture of per-chloride of iron in 10- to 20-minim doses, frequently administered, is a useful

remedy. Local treatment is of great service in relieving the troublesome symptoms of acute tonsillitis. The treatment is both antiseptic and sedative. The sedative treatment may be carried out by the application of hot fomentations to the throat, glycerin of belladonna being painted on to the skin. In some cases it is sufficient to rub the skin and the neck with liniment of belladonna, subsequently tying a flannel round the neck. Sedative applications to the throat itself are useful in allowing the patient to swallow, and for relieving the pain. The best of sedative applications is a solution of hydrochlorate of cocaine, 5 to 10 grs. to the ounce, painted on to the tonsils just before food is administered. Cocaine lozenges may also be given in moderation. The sucking of ice is also a useful sedative. Other local applications to the throat are useful for washing away the secretion, and acting as antiseptics. If the patient may gargle, he can use either a solution of chlorate of potash (100 gr., dilute hydrochloric acid 100 minims, syrup 4 dr., water 10 oz.), or the throat may be sprayed with a solution of bicarbonate of sodium and borax (10 gr. to the ounce), and of carbolic acid ($\frac{1}{2}$ gr. to the ounce), or with a dilute mercurial spray (1 in 5000 of corrosive sublimate).

Frequently in the early stages of acute tonsillitis, it is highly beneficial to paint the throat once with a solution of nitrate of silver (10 to 20 grs. to the ounce). This procedure, in cases of mild infection of the tonsil, undoubtedly cuts short the disease. The throat may also be painted with glycerin of carbolic acid (1 in 20) or glycerin of corrosive sublimate (1 in 2000). If an abscess forms, it sometimes bursts spontaneously, but may be frequently ruptured with the finger-nail, or it may be opened by means of a knife.

FOLLICULAR TONSILLITIS.

Acute follicular tonsillitis is, like acute tonsillitis, an infection which may either result from a catarrh of the follicles, or an acute inflammation of them, due to one or other form of coccus. It usually occurs in children, and in its acute form presents practically the same symptoms as acute tonsillitis. The treatment is also practically the same, except that it is sometimes beneficial to treat the suppurating follicles individually with solution of nitrate of silver.

On examination, patches are seen over the tonsil, which suggest, in some cases, a diphtheritic infection, but the diagnosis is made by the same method as in acute tonsillitis; the treatment is also practically the same.

CHRONIC TONSILLITIS.

This is a chronic enlargement of the tonsils, which may result from many causes.

Etiology.—The affection may arise from acute, simple, or follicular tonsillitis, or may be chronic from the first. In the first case, repeated attacks of acute or subacute tonsillitis lead to the enlargement, which is due to fibroid thickening of the tonsillar tissue, with some increase of the lymphoid cells. In chronic inflammation there is frequently a progressive enlargement of the tonsils, sometimes more marked on the one side than the other, so that they may even meet in the middle line. The surface of the tonsils may be smooth, but is more usually pitted, and the tonsillar

crypts may be completely destroyed, being shown only by shallow markings on the surface of the tonsil. The degree of change varies: thus there are hard tonsils and soft boggy tonsils. They may be pale, or slightly congested on the surface, this surface congestion frequently leading to small hæmorrhages. The uvula, at the same time, is frequently elongated, and there may be coincident pharyngitis, which is kept in a subacute condition by the enlarged tonsils being in front of the pharynx, and thus blocking in the secretion.

Chronic tonsillitis is a very frequent disease in children and young adults, and the symptoms it presents are very characteristic. The child walks frequently with the mouth open, and sleeps in the same condition; the voice is nasal, and there is frequently some difficulty of respiration; cough is often present, and in some cases—especially in adults—it may be excessive, especially in young women with a neurotic temperament. The cough is short, hacking, or barking in character, and is sometimes accompanied by a glairy expectoration. It is not infrequently severe in the early morning, and bleeding is not uncommon, the pillow of the child being stained with blood, or the lips and gums being found covered with blood in the morning. Children suffering from chronic tonsillitis frequently lose their appetite, become pale and flabby, and lose flesh, while the bowels are usually constipated.

One of the chief features in children is the tendency to bronchitis which they exhibit; in many cases the bronchitis is kept up by the enlargement of the tonsils, and so much so that it is not until they are removed that the bronchitis is cured. In cases of prolonged enlargement of the tonsils, usually with repeated attacks of bronchitis, but sometimes without, deformity of the chest may ensue, either with a flattening or more commonly the "pigeon breast." Enlarged tonsils may be associated with tuberculosis, but there is no evidence that the association is other than accidental. In some cases, however, there are enlarged glands at the angle of the jaw, associated with enlarged tonsils, and these glands are eventually found to be tuberculous, there being usually no tuberculous lesion to the tonsil itself. This only means that the tuberculous infection has taken place through the tonsil or pharynx, and infected the glands of the neck.

Course, prognosis, and treatment. — The course of chronic tonsillitis in children is a very variable one. It is usually associated with some anæmia, wasting, and disordered digestion; and, as has been stated, more especially in the winter, it is associated with recurrent attacks of bronchitis. In many cases, simply by a general tonic treatment, cod-liver oil, iron, and maltine, as well as by treatment directed to the relief of the bronchitis, such patients do well, and the tonsils diminish in size, although this may take some months to accomplish. The local treatment which is to be employed is the use of astringents, in the form either of tincture of iron and glycerin (1 drm. of the tinctura ferri perchloridi to 1 oz. of glycerin), or tannin and glycerin (10 grs. to the ounce). If there is much irritation of the throat, glycerin with borax may be used instead of astringent lotions, or a solution of iodine and iodide of potash, or of menthol and olive oil (10 to 20 grs. to the ounce) may be used, or the menthol may be applied in a spray form, after dissolving in parolein.

The question of the removal of the tonsils frequently arises, and with regard to this it may be said that, apart from the existence of adenoids, the tonsils may themselves give rise to obstruction to the respiration, as for

example when they nearly meet in the middle line. In these cases their removal is essential for the improvement of the patient, as well as for the relief of the bronchitis. In not a few cases, however, recovery takes place without the removal of the tonsils, and even when the tonsils have been removed they frequently become large again. The indications for the removal are when they interfere with the respiration, and when there is much pharyngeal and post-nasal inflammation, with some degree of deafness. The effects of removal, however, are, as has been indicated, frequently disappointing. The tonsils may remain large many years, up to the age of puberty, when they tend to diminish; but in some cases their enlargement persists in young adult life.

<div align="right">SIDNEY MARTIN.</div>

DISEASES OF THE PHARYNX.

PHARYNGITIS.

PHARYNGITIS is a condition of inflammation of the pharynx, and may be associated with some acute diseases of the tonsils and fauces, as in diphtheria, scarlet fever, and measles, and it may also exist by itself in a catarrhal form, acute or chronic, and may in one form be chiefly shown by an enlargement of the lymphoid tissue, as in granular pharyngitis.

In acute pharyngitis the mucous membrane is dusky red in colour, is swollen, and is covered on the surface with a layer, frequently very tenacious, of mucus-containing pus cells, but not, as a rule, blood. There are well-marked signs of irritation of the throat, not so much in the form of cough as in a feeling of stiffness, of pain in deglutition, and of a tendency to repeated acts of swallowing, which increase the distress. There is hawking of phlegm, which is difficult to remove, and in consequence vomiting is not infrequent. A slight degree of fever is sometimes associated with the condition, but it does not last long.

The treatment in the initial stage is by the administration of a mercurial purgative and the application of sedative sprays or lotions. Gargling is not of much value, inasmuch as it does not completely reach the pharynx; but the application of hot sprays, or a cold spray containing bicarbonate of sodium (10 grs. to the ounce) is very beneficial. Sedative lozenges, such as cocaine, are of use.

Acute simple pharyngitis may lead to œdema or ulceration, or pass into the chronic form; it may simply be an exacerbation of the chronic condition.

In chronic pharyngitis the catarrh leads to several different conditions. There is a continuous secretion of mucus in some cases, in others a greatly diminished secretion. In the first case the epithelium is more or less intact, and is proliferating, and in the second case the epithelium is partly detached, and is deficient in vitality.

Chronic inflammation leads to fibrosis of the mucous membrane, to a dilatation of the small venules in the pharynx, and generally to a condition of atrophy. In chronic pharyngitis several varieties may be distinguished, such as pharyngitis sicca, or dry pharyngitis; pharyngitis atrophica; and granular pharyngitis. In the last case the stress of the inflammation is on the follicles, which enlarge, forming raised patches, frequently coalesce,

forming projecting masses, glazed on the surface. There may be dilated vessels, which sometimes give way, causing hæmorrhage. The amount of blood lost is, however, never large, being limited to streaks or spots in the mucus expectorated.

Chronic pharyngitis in a moderate degree may not give rise to many symptoms, except that occasionally there are exacerbations leading to the symptoms of subacute pharyngitis. In other cases it leads to great distress in speaking, singing, and, to some degree, in swallowing. An accumulation of mucus on the surface, especially in the upper part of the pharynx, leads to hawking, and even vomiting, in the morning. Chronic pharyngitis frequently spreads downwards to the epiglottis, to the ventricular bands, and to the vocal cords, leading to hoarseness and aphonia.

The treatment is directed to improve the chronic catarrhal condition by attending to the general health, and by the application of astringents, either in the form of spray, or of paint, and of sedatives, such as menthol and cocaine if there is much distress. Caustics may be applied to the follicles when they form large masses. It is sometimes, however, an obstinate condition, and frequently treatment is of but little avail, the patient only recovering on removal to a dry climate.

<div align="right">SIDNEY MARTIN.</div>

DISEASES OF THE ŒSOPHAGUS.

THE œsophagus is about 9½ in. long, and extends from the pharynx to the stomach. The commencement is 6 in. from the incisor teeth, and opposite the sixth cervical vertebra: the termination is 15½ in. from the incisor teeth and opposite the tenth dorsal vertebra, corresponding in front to the level of the ensiform process. When quiescent, its walls are opposed to each other, the mucous membrane lying in longitudinal rugæ. It lies at first behind, and then to the left side of the trachea, passing down in front of the vertebral column. It is supplied with nerves from the vagus and sympathetic. In structure it is possessed of three chief coats. There is a thin external connective tissue coat; next to this is the muscular coat, composed of an inner thick circular layer with an outer thin longitudinal layer. The upper third of the œsophagus contains striped muscular fibres; in the lower two-thirds these are unstriped. The submucous coat consists of connective tissue, which contains blood vessels, lymphatics, and glands. These latter open out in the mucous membrane, which is composed of epithelium, and separated from the submucous by a thin muscular coat, the muscularis mucosæ. The act of deglutition, which is voluntary as far as the pharynx, is involuntary when the pharyngeal muscles contract over the swallowed mass. The contraction of the pharynx passes this on to the œsophagus, which by its peristaltic action continues it on to the stomach. This peristaltic movement is not stopped even when the œsophagus is ligatured, or when a portion of it is removed. The motor nerve of the œsophagus is the vagus, and if this be divided the food collects in the lower part of the gullet. The afferent nerve fibres of deglutition are the palatine branches of the fifth cranial nerve, and the pharyngeal branches of the vagus. In disease the œsophagus is also capable of a reverse peristalsis.

The œsophagus may be examined by the passage of a bougie, or by means of the sounds heard in the stomach and produced by a swallowed bolus. When solid food is swallowed, two sounds are heard by the stethoscope placed over the stomach. The first is produced by the bolus entering the stomach, and the second at the end of swallowing, when the remaining part of the bolus is squeezed through the cardia. Normal deglutition lasts about six seconds. No sound is heard over the healthy stomach when water alone is swallowed, unless it be mixed with air. The examination of liquids regurgitated from the œsophagus sometimes yields important results, inasmuch as the food never having entered the stomach, it has not been exposed to the action of the gastric juice. The regurgitated mass does not, therefore, contain peptones (unless these have been administered in the food), and is alkaline. If the regurgitated liquids contain free hydrochloric acid, as shown by the tests described under "Diseases of the Stomach," p. 651, the liquid must have come from the stomach. Passage of the sound is a usual method in the examination of the diseases of the œsophagus, especially when a stricture is suspected. The same precautions which are taken for the passing of the sound in diseases of the stomach, must be observed when it is used for the œsophagus; especially must the evidences of thoracic aneurysm be sought for before the instrument is used. The sound may pass easily into the stomach, as in cases where there is no stricture. It may be held by the stricture, and with gentle pressure the resistance may be overcome, as in cases of spasmodic stricture; or it may be prevented from entering the stomach by an organic stricture. In the latter case, on removal, the sound may be covered with mucus or blood; but not infrequently in cancer, most of the bleeding occurs afterwards.

The œsophagus being a portion of the alimentary tract in which food remains but a very short time, it is rarely the seat of infective disease. Tuberculous ulceration is of extreme rarity. Syphilitic ulceration, producing stricture, has been observed. The diphtheritic membrane may, in rare cases, extend from the pharynx down the œsophagus, but as a rule infective diseases do not spread from the pharynx to the œsophagus. The gullet may be the seat of aphthæ, spreading from the mouth.

The diseases which will be discussed are—(1) the results of injury, due to the presence of foreign bodies, or to the swallowing of corrosive substances and hot liquids; (2) diverticula; (3) dilatation without stricture; (4) stricture, spasmodic and organic (simple or malignant).

INFLAMMATION.

Œsophagitis, or inflammation of the gullet, is the result of injury, of infection following a new growth, or of the extension of surrounding inflammation.

Perforation of the gullet occurs from foreign bodies, from new growths, or by the opening of a tuberculous abscess (usually globular), or an aneurysm into the gullet.

Impaction of foreign bodies in the œsophagus leads to ulceration of the wall, with frequently an infection of the coats, and a diffuse cellulitis outside, with or without perforation. Pleurisy may also follow impaction of a foreign body, ending in effusion or empyema. The treatment and other results of foreign bodies need not be here discussed.

The swallowing of corrosive substances (mineral acids or caustic

alkalies) leads to inflammation and ulceration, and subsequently stricture of the œsophagus.

The initial symptoms to which swallowing of these substances gives rise, is a sense of burning pain along the œsophagus, in the neck, behind the sternum, and in the back. The chief pain is not infrequently ascribed to the region of the manubrium. When the severe symptoms have passed off, the patient may experience no further trouble, and it will not be till some time afterwards that difficulty of swallowing is experienced. It is first shown in the difficulty of getting solid food into the stomach, the patient stating that it sticks at one part. Regurgitation of food then follows to a greater or less extent; and an examination by means of the bougie shows that there is stricture at one or other part of the gullet. The treatment in such cases is by means of gradual dilatation of the stricture by the use of bougies; in this way the stricture may be sufficiently dilated to allow the proper amount of food to be swallowed. In some cases, however, the stricture is practically impermeable, and gastrostomy has to be performed. Such patients are liable to die of starvation.

DIVERTICULA.

A pressure pouch of the œsophagus is a rare condition. It consists in a pouch, of greater or less size, being formed at the junction of the pharynx and œsophagus. Such pouches have been described as possibly due to defective development, as in the case of Meckel's diverticulum of the small intestine. In other cases they have been ascribed to a lesion of the mucous membrane, produced by a foreign body, and subsequent formation of a pouch by pressure from within. The pouch, which is formed in the position above described, projects at the back of the gullet, and bulges on both sides of the neck; in some cases, however, only on the left side. The recognition of this as a pressure pouch is by observing that it is larger after a meal; that gas and particles of food can be pressed out of it; and that food returns for some time—perhaps hours—after a meal, in an undigested condition, the return of food being associated with coughing or some such act. Owing to the pressure of the distended pouch on the œsophagus, there is difficulty of swallowing, and the passage of a sound shows that there is no organic obstruction to the gullet. In the cases which have been recorded, the pouch has lasted for many years, and death has been due to some other cause. In others, however, death has been partly due to starvation from pressure on the gullet. Pressure pouches are such rare conditions, that their treatment is a matter of discussion; but the proper treatment seems to be that performed by v. Bergmann, and done once in this country by Butlin; it is the performance of an operation for the removal of the pouch. Both in v. Bergmann's and Butlin's cases, complete recovery followed the operation. Gastrostomy has been performed when the pressure on the œsophagus has been very great. This cannot be considered a treatment at all comparable to the removal of the pouch, as this cures the condition.

DILATATION.

This is also a very rare condition of the œsophagus, but it does occur, and may cause death. Thus, in one case, a patient, a female, æt. 35, was admitted into the hospital for difficulty in breathing. The history of the case showed that it was one in which the chief symptoms were attacks of vomiting, and pain in the upper part of the abdomen. These attacks came on at intervals. While she was in the hospital, dyspnœa and regurgitation of food were the chief symptoms observed. Dyspnœa was shown by marked stridor, especially after exertion, and there was frequent cough, brassy in character, with slight expectoration. The breath sounds were somewhat stridulous over the left apex. The presence of a mediastinal tumour was suspected, though there was no other evidence of it. There were no physical signs in the abdomen. The patient died from exhaustion and dyspnœa. The post-mortem examination revealed somewhat recent pleurisy of the right side, and some recent broncho-pneumonia in the right lower lobe. The only condition accounting for death was a greatly distended œsophagus; the enlargement extending the whole length of the tube, the greatest transverse diameter being $5\frac{1}{2}$ in. The swelling was pyriform, and bulged into the right pleura and into the pericardium, but it did not produce any evident compression of the trachea. It contained a large quantity of undigested food. There was no stricture of the cardia, and no new growth. The walls of the gullet were thin, except the mucous membrane; the epithelium was irregularly thickened throughout, and showed in many places superficial erosions, evidently the result of the pressure of the contained food. Microscopical examination of the gullet showed that there was fatty degeneration of the striated muscle fibres of the upper third, and in the lower two-thirds the unstriated muscle showed signs of atrophy. There was no sign of fibrosis of the wall, nor of any chronic inflammation. Other cases have been published showing the same symptoms. The origin of the disease is obscure. The only explanations which appear probable, are, that it is a primary nerve defect, since accumulation of food in the œsophagus, with subsequent dilatation of it, is produced by secretion of both vagus nerves, or that it is due to persistent spasm of the cardia.

STRICTURE.

Stricture of the œsophagus is either spasmodic or organic. In the latter case it is either simple stricture, due to cicatricial contraction, or malignant, due to epithelioma. What may be called false stricture of the œsophagus is produced by pressure upon it, either by thoracic aneurysm, by a new growth in the mediastinum, or by a very large pericardial effusion.

Spasmodic Stricture

is due to spasm of the muscular coat; it is sudden in onset, and occurs in a paroxysmal manner. The patients who complain of it are usually hysterical females or hypochondriacal men. There may be pain, and regurgitation of food is common. It is not usually associated with wasting, although cases have been described where great wasting has occurred, and even death has followed starvation. The passage of a bougie clears up the

case, as by gentle pressure the spasm is overcome, and the stomach is entered by the bougie. The passage of the bougie under chloroform-narcosis may be advisable in some cases. The treatment is that employed for nervous conditions generally, namely, the moral persuasion of the patient, the administration of tonics, and the regulation of the mode of life.

MALIGNANT STRICTURE.

The stricture of the œsophagus, due to cicatricial contraction, has already been considered, and it now remains to discuss stricture due to the development of a new growth in the walls of the gullet. The kind of new growth is almost invariably squamous epithelioma. It occurs most frequently in the lower third of the œsophagus, producing a stricture near the cardiac orifice of the stomach. Next, most frequently it occurs in the upper third, and is least common in the middle of the œsophagus. In its growth it slowly contracts the lumen of the gullet, and above the constriction the walls dilate and hypertrophy. The amount of dilatation and hypertrophy present depends upon the slowness of the development of the growth and the amount of stricture produced. With some forms there is rapid ulceration, and but little hypertrophy is produced. The extent of the growth, which arises in the mucous membrane, varies at death. It may extend over two or three inches, and tends to infiltrate the walls and to spread upwards and downwards along the mucous membrane. It does not commonly, however, extend from the cardia far into the stomach, nor in the upper third does it extend into the pharynx. Perforation may occur into the cellular tissue of the neck or posterior mediastinum, or into the trachea or pleura, usually of the left side, and is as a rule produced by septic ulceration of the walls of the gullet above the cancer. When it has occurred, it leads, in the cellular tissue, to a diffuse cellulitis, ending either in suppuration or in gangrene. The cellulitis may spread down the neck into the thorax, and may produce acute pericarditis or gangrene of the upper part of the lung. It may also, as in one case observed, produce a thickening of the sides of the larynx, involving the recurrent laryngeal nerve, thus causing paralysis of one vocal cord. Perforation into the trachea is not so common, but may lead to septic broncho-pneumonia. Perforation into the pleura causes empyema, often putrid in character. Perforation may also occur into the aorta, producing death from hæmorrhage; or into the pericardium, producing acute pericarditis. Secondary growths may occur in the glands near the gullet, more rarely in the organs of the body, sometimes the liver. In cancer of the œsophagus, death occurs partly from starvation and partly from the complications of perforation, which have just been described.

Symptoms.—Cancer of the œsophagus occurs in middle age (40 to 50 years), usually in men, and the symptoms are, as a rule, definite. They are very insidious in origin; the first symptoms the patient complains of being, as a rule, a gradually increasing difficulty in swallowing solid food, liquids being swallowed at first with ease. This difficulty varies from time to time, but gradually increases until no solid food is taken. The patient frequently comes for advice at this period, and it is found, on testing his powers of swallowing, that the swallowed food regurgitates after a time in an undigested and still alkaline condition, showing that it has not entered the stomach. Associated with the difficulty of swallowing is great wasting, and the symptoms, which have perhaps lasted two or three months, may

have been attended by a loss of two or three stones in weight; otherwise, there may be no cancerous cachexia. Indeed, some of these patients at this time preserve their fresh complexion. Later on it gives place to the sallowness of cancerous disease. An examination by the œsophageal bougie must now be made, and it is found that this does not pass into the stomach, but is held some distance down the œsophagus. On withdrawing the bougie, it may in some cases be found to be covered with particles, which on examination show cancerous cells, or it may be covered with blood, and its use is frequently followed by slight bleeding; or it may in some cases be covered with mucus, and its use be followed by the discharge of a large quantity of thick unpigmented mucus. From this combination of symptoms the diagnosis of stricture of the œsophagus can be made. The sensations which the patient complains of at this time, apart from those of swallowing, vary to some extent. Pain is present, referred to the chest, to the back, or to a particular point behind the sternum. But pain is not a marked feature in cases of cancer of the gullet. The sensations following swallowing are frequently located to the region of the manubrium of the sternum, or to the end of the sternum, that is, the upper part of the epigastrium. A tumour can rarely be felt, even when the disease is situated in the neck. If a patient be seen in the later stages, emaciation may be extreme, but the chief points which give rise to the difficulty in the recognition of the disease lie in the presence of complications. Thus the patient may present himself for the first time with the symptoms and signs of pleuritic effusion or empyema, and unless a careful history be taken in such cases, the primary disease is apt to be missed. In cases of diffuse cellulitis of the neck, also, the local disease may be unrecognised, especially when the upper part of the lung is affected. In some such cases paralysis of the vocal cord may occur, and the diagnosis from thoracic aneurysm or mediastinal tumour may be extremely difficult, if not impossible, until a post-mortem examination is made. Similarly, too, if the malignant ulcer produces a septic bronchitis by ulceration of the trachea, the signs and symptoms of this may obscure the primary disease, as well as in the case, in which a subphrenic abscess is the result of perforation of the cancerous ulcer. The only way in which these conditions can be diagnosed as secondary to cancer of the œsophagus, is by careful attention to the history of the case and by an examination of the œsophagus by means of a sound.

Diagnosis and prognosis.—The diagnosis of cancer is made from the following points: its occurrence is usually in a man of middle age, the symptoms of stricture, that is, of the difficulty of entrance of food into the stomach and of its regurgitation; and the recognition of this stricture by the use of the œsophageal bougie. Diagnosis is aided, in some instances, by auscultation of the swallowing sounds; the second sound is described as being absent in stricture of the œsophagus. The disease is associated with great emaciation, which is due more to the starvation induced than to the cancerous disease itself.

Cancer of the œsophagus is always fatal, and the duration is somewhat less than that of cancer of the stomach, inasmuch as the starvation is greater, and complications, such as perforation and fatal hæmorrhage, more frequently occur.

Treatment.—The object of treatment is palliative, namely, the relief of pain by the administration of sedatives, such as morphine, and the adoption of means for getting more food into the stomach, as by this means

the patient's condition is greatly improved. It is possible, in many cases, to pass a small tube through the stricture, and this may be kept in position and the patient fed continually through it. In other cases it need not be kept in position, but only passed when food is required. Gastric digestion is, as a rule, good, and therefore the patient can take a large amount of food. Gastrostomy has been performed in order to feed the patient more effectually. It cannot, however, be said to have any advantages over feeding by the tube, if this is possible. Feeding by the tube has one danger, namely, that of perforation of the soft walls of the gullet above the cancerous infiltration, and this has occurred not infrequently, so that the catheter has passed into the pleural cavity, causing death by septic inflammation. Where feeding by the tube is impossible, gastrostomy is not considered advisable, and feeding by the rectum is to be adopted in the manner described in the article, "Diseases of the Stomach." The course, however, in spite of all treatment, is usually a progressively downward one

SIDNEY MARTIN.

DISEASES OF THE STOMACH.

A DISCUSSION of the diseases of the stomach is necessarily preceded by a short account of the anatomy and physiology of the organ; for without the former a correct appreciation cannot be formed of the changes which can be discovered by physical signs in organic diseases of the stomach; and without the latter no clear ideas can be formed of the changes in functional disease of the organ.

INTRODUCTORY.

The stomach is a pear-shaped bag, almost completely surrounded by peritoneum, lying in the upper part of the abdominal cavity, and extending from below the left vault of the diaphragm to the right side of the vertebral column. It is divided artificially into a cardiac and pyloric region, an anterior and posterior surface, and a lesser and greater curvature. In size it varies according to age and sex, and in each individual at different times, according to the degree of distension. When fully distended it is about $9\frac{1}{2}$ to $10\frac{1}{2}$ in. in its longest diameter, and 3 to $3\frac{1}{2}$ in. from before back; while the average capacity of the adult stomach is a little over a litre, or from 35 to 40 oz.; the variations, however, which have been found by Ewald, are from 9 to 59 oz. A capacity of more than 3 pints must be considered as pathological.

In its natural position the stomach lies almost vertically, the cardiac orifice being situated $15\frac{1}{2}$ in. from the incisor teeth, and on the left side of the body of the tenth dorsal vertebra, and in a line with a point 1 in. from the sternal insertion of the seventh left costal cartilage. The lesser curvature extends from the cardia vertically, along the left side of the bodies of the tenth, eleventh, and twelfth dorsal vertebræ to the pylorus, which is situated on the right side of the first lumbar vertebra; this is opposite a point in the epigastrium below the xiphisternum and just

outside the parasternal line. The stomach is held in position by the œsophagus and by the duodenum, as well as by the folds of the omentum attached to it. The lower limit of the greater curvature of the distended stomach in the normal individual is marked by a transverse line between the cartilages of the ninth ribs or sometimes the tenth. This is two fingers' breadth above the umbilicus. The anterior surface of the stomach touches the liver, the diaphragm, and, below, the anterior abdominal wall. The posterior surface of the stomach touches from above down the diaphragm, spleen, kidney, pancreas, and mesocolon.

The four coats of the stomach are peritoneal, muscular, submucous, and mucous. The three layers of the muscular coat are the external longitudinal, the circular, and the slightly developed oblique coat. The mucous coat is separated from the submucous by the muscularis mucosæ. It is composed of two classes of glands, cardiac and pyloric. The former contain two kinds of cells—small central cells secreting pepsin, and large parietal cells secreting hydrochloric acid; the pyloric glands secrete no acid, only pepsin.

The stomach is richly supplied with blood vessels from the cœliac axis and from the splenic artery. The nerves are the vagus and the sympathetic; the right supplies the posterior, and the left the anterior surface.

One of the most important physiological aspects of the stomach lies in its nervous mechanism, because in not a few cases of disease it is evident that the nervous system exercises a profound effect on the processes of the stomach, and the interaction of both leads, in some cases, to very great disorder. Although this is so, the effect of the nervous mechanism of the stomach is by no means clear from a physiological point of view. The vagus nerves, for example, have been shown to exercise some power over the movements of the organ, and a section of both causes pallor of the mucous membrane during digestion. Stimulation, however, of the vagus does not produce secretion of gastric juice—although gastric juice flows as the result of local stimulation, whether mechanical, chemical, or electrical—yet the flow is influenced by the higher nervous centres, since it may be excited reflexly by a flow of saliva. The stomach, however, does not possess a direct motor nerve nor a direct secretory nerve, but both motion and secretion are to some extent under the influence of the nervous system. When removed, the movements still persist in an appropriate warm chamber. It has been supposed that the local nervous mechanism of the stomach, as shown by its automatic action, resides in Auerbach's plexus and ganglia, situated in the muscular coat.

In connection with the nervous mechanism of the stomach, vomiting must be considered. It is a reflex effect, dependent on the excitation of a centre in the medulla oblongata. This may be directly affected; although more usually it is affected reflexly by impulses either from the fauces and the surrounding parts, or from the internal organs by means of the visceral nerves supplied to them. In some cases, as when vomiting is accompanied by great pain, the afferent nerve is a sensory one.

The physiological processes which occur in the stomach may be divided into mechanical, chemical, and absorptive.

1. The movements of the stomach may be divided into two periods. In the first period the food is intimately mixed in the stomach by means of the circular and churning movements, the food passing from the cardia along the greater curvature and back again along the lesser. After the food is swallowed, this period lasts a considerable, although varying, time,

dependent chiefly upon the size of the meal. In the second period of movement the semi-digested food or chyme is propelled, probably *en masse*, into the duodenum, although small portions of the liquid may from time to time be expelled. The movements of the stomach are diminished by violent exercise and strong emotions, and cease during sleep.

2. The chemical processes of the stomach are concerned with the action of gastric juice on the mixed food—the proteids, fats, and carbohydrates taken in the meal. The gastric juice possesses three actions—first, it curdles milk, due to the milk-curdling ferment, rennin; second, it digests proteids by means of pepsin acting in conjunction with hydrochloric acid; third, it is antiseptic owing to the presence of this acid. The gastric juice has no action on fats or on carbohydrates; it stops the action of the saliva on starch, although this goes on in the stomach, in some cases, for a period not exceeding·forty minutes. The milk-curdling ferment precipitates casein in finely divided particles previous to its digestion by the pepsin hydrochloric acid. The action of this combination is exerted solely on proteids or albuminous substances, which are transformed from insoluble substances, or substances which are not assimilable by the organism into soluble proteids—first into albumoses, and then peptone. Gelatin is also digested in the stomach. The result of the action of the gastric juice on the mixed food, as well as the movements of the organ, is that the food is partly digested in the manner described, and is finely divided, the fat being set free and floating on the surface of the contents of the organ. In addition to this, an important change takes place, from the fact that the organic acids are liberated from their salts by means of hydrochloric acid. The hydrochloric acid which exists in the stomach contents is found in two forms— as chlorides taken in with the food; and as free hydrochloric acid, which is secreted in the gastric juice. But if there is proteid food in the stomach, some of this hydrochloric acid combines loosely with it, while the excess remains free, and this is an important point, because the loosely combined hydrochloric acid does not give the colour tests of free hydrochloric acid.

Many foods contain organic acids in the form of salts, and especially lactic acid. Meat, for example, contains sarcolactic acid, and bread also contains lactic acid. If both these foods are taken, free lactic acid is found in the stomach contents, as well as free hydrochloric acid; but after a short time, varying from one to two hours, the lactic acid is absorbed, and hydrochloric acid alone remains. The presence of lactic acid gave rise to the idea that it was secreted in the gastric juice. There is but little doubt that its presence in any quantity actually inhibits the initial secretion of free hydrochloric acid; and, moreover, the pepsin does not act so readily in the presence of acetic, lactic, and butyric acids as in the presence of hydrochloric acid.

The duration of digestion of a meal depends on many factors, some of which are inherent in the individual, others of which are dependent on the size of the meal taken, with its accessories. The complete digestion of a meal consisting of soup, a large beef steak, and bread with water, takes from five to seven hours, at the end of which time the stomach is practically empty, the contents being a little neutral liquid containing a few flakes of mucus. Smaller meals will require less time, and the rapidity of the early processes of digestion is greatly influenced by the amount of alcohol taken. This retards the processes in excess; but if the quantity of alcohol taken be moderate, the digestion is completed in as short a time as when no alcohol is taken.

3. The absorptive processes which take place in the stomach concern sugar, salts, and proteids. The sugar is that which is formed by the action of the saliva on starch; the salts are those which are taken in with food, and there is probably an active interchange between the salts of the blood and those of the gastric contents during digestion. Although most of the digested proteids are expelled into the small intestine, for the further action of the pancreatic juice and the bile, yet some amount of the albumoses and peptone is absorbed by the gastric mucous membrane, being transformed during the process into the proteids of the blood. The question of the absorption of water in the stomach is an important one, and it has been shown by Tappeiner and von Mering, that but little water is absorbed in the stomach. This agrees with what we know of the process of digestion in the stomach, since during digestion the stomach is practically a closed bag, and a certain proportion of water is a necessity for the proper carrying out of the process. Most of the water is absorbed in the large intestine.

The proper carrying out of digestion depends, as regards the stomach, first, in the secretion of a sufficient amount of gastric juice, which gradually increases in acidity to a percentage of 0·2 of hydrochloric acid; second, on the continuance of the movements of the stomach, which begin as soon as the food enters the organ, and cease upon the expulsion of the contents into the duodenum; third, on the character of the meals, and on a certain interval being allowed between the meals for the digestion to be completed. In modern life there is no doubt that some individuals train their stomachs to eat large and unsuitable meals, but this always leads eventually to disorders of digestion and nutrition.

Methods of examination.—The stomach contents have to be examined for the presence of undigested food; the presence of micro-organisms, and of mucus, pus, and blood; the total degree of acidity, and as to the nature of the free acids present, namely, hydro-chloric, lactic, butyric, and acetic acid; the presence of the products of digestion, albumoses and peptone; and the presence of pepsin and the curdling ferment. For the presence of bacteria, a cover-glass preparation dried and stained with methylene-blue is usually sufficient. Sarcina is, however, best stained with a very dilute solution of gentian-violet. Mucus from the stomach is stringy and tenacious, and differs from that coming from the lungs in being unpigmented; it may contain streaks of blood, or the blood may be diffused through it, giving a faint yellow colour. It is soluble in liquor potassæ or baryta water, and is precipitated from this solution by acetic acid. Pus is sometimes present in vomited matters, and is recognised, either unstained under the micro-scope, or by making a cover-glass preparation, and staining with Löffler's methylene-blue. The detection of blood is, in some cases, important. The microscope may at once decide the presence of blood corpuscles. The guaiacum test may be applied, but inasmuch as it is given by some vegetable substances, for example potato, and by bile and saliva, it is not of much value in detecting blood in vomited matters. "Coffee-ground" vomiting must be diagnosed from vomit containing bile or vegetable-colouring matter. The best test to apply for the detection of blood in this case, is the formation of hæmin crystals, or the production of Prussian blue. For the formation of hæmin crystals, a little of the black sediment is put on a microscope slide and mixed with a little common salt. One or

two drops of glacial acetic acid are added; and the specimen is covered with a cover-glass, and heated over a spirit-lamp until it bubbles. The hæmin crystals are reddish brown and oblong. The test, however, may fail, and the second must be applied. To some of the black sediment in a porcelain capsule a small quantity of potassium chlorate is added, and a few drops of hydrochloric acid; on heating, with the addition of a few drops of potassium ferrocyanide solution (5 per cent.), Prussian blue is developed, if blood is present. The patient must not, of course, be taking any preparation of iron.

The total acidity of the stomach contents may be due to acid salts, to hydrochloric acid, or to organic acids. Litmus paper is a test for acidity; Congo red paper, which is turned blue or violet-black, is a test of free acidity, whether due to hydrochloric acid or to organic acids. The blue colour disappears on the addition of ether in the case of the organic acids, but is permanent when produced by hydrochloric, or any other mineral acid. The total acidity is estimated by taking 20 c.c. of the stomach contents, adding three or four drops of a saturated alcoholic solution of phenolphthalein, and diluting with water to 300 c.c. 150 c.c. of this are placed in each of two flasks, and to one a decinormal solution of sodium hydrate is added, until a red colour appears. The liquid is now neutralised, and the determination may be controlled by a second estimation in the other flask. Each 100 c.c. of the sodium hydrate solution neutralise 0·365 grm. of hydrochloric acid. If, therefore, 50 c.c. of the solution be required to neutralise 100 c.c. of the stomach contents, the total acidity expressed in terms of hydrochloric acid is equal to about 0·18 grm. per cent.

Free acidity may be divided into fixed acidity, due to hydrochloric acid or lactic acid; and volatile acidity, due to butyric or acetic acid.

Hydrochloric acid (other than in combination as chlorides) in the gastric contents exists in two forms—in a free state, and combined with proteids. This latter combination does not give the colour reactions which will be described, and it can only be estimated by one of the methods for the total estimation of hydrochloric acid. The best tests for the detection of free hydrochloric acid are two, which give the same colour reaction, namely, Gunsberg's and Boas'. Gunsberg's solution is composed of phloroglucin, 2 grms.; vanillin, 1 grm.; alcohol, 30 c.c. Boas' solution consists of 5 grms. resorcin, 3 grms. of cane sugar, and 100 c.c. of weak spirit. Both tests are applied in the same way, namely, a drop of the solution is mixed with a drop of the stomach contents in a white porcelain capsule, and evaporated to dryness. If free hydrochloric acid is present, a rose colour is developed. As little as 0·05 grm. per cent. may be detected in this way. Lactic acid, the other fixed acid, is best detected by shaking up the stomach contents with an equal volume of ether; on removing the ether and allowing it to evaporate, the residue may be dissolved in water. The tests to be applied are—first, Uffelmann's reaction. A solution is made of carbolic acid (1 to 20) 10 c.c., and water 20 c.c. One or two drops of liquor ferri perchloridi are added, and the amethyst blue solution is changed to a clear yellow or greenish yellow by as little as 0·01 per cent. of lactic acid. A second test is made by adding one or two drops of liquor ferri to 50 c.c. of water. This solution is almost colourless, and is made yellow by lactic acid. Volatile acids may be detected by the smell, that of butyric acid being very characteristic; or by the formation of their respective ethers, namely, by adding to the stomach contents a small quantity of alcohol, 2 drops of sulphuric acid, and heating. Butyric ether has the smell of pine-apple

rum; acetic ether has the smell of new-mown hay. Acetates give also a blood-red colour with a solution of perchloride of iron. For the methods of determination of the total quantity of hydrochloric or organic acids, other works should be consulted.

The presence of digestive products (albumoses and peptone) in the stomach contents is detected by the biuret reaction, which is a pink colour, developed on adding a trace of solution of copper sulphate and an excess of potash to the liquid.

The activity of the gastric juice and the power of the stomach to manipulate food and to empty itself in a certain time are determined by means of a test meal. The secretion of the gastric juice may be tested by using Ewald's test breakfast, consisting of a little over 1 oz. of bread and about 12 oz. of water. This is removed by means of the stomach sound in from half an hour to an hour; and the presence of hydrochloric acid is detected in the manner previously described. A better test meal, which also tests the mechanical power of the stomach, is that of Leube, and consists of a little soup, 5 oz. of beef steak, and a small bread roll. The patient must be fasting, and must rest after the meal. In five hours the stomach contents are removed by the sound. Usually the meal is in greater part digested, and in seven hours, in healthy individuals, it is completely so. It is in some cases advisable to use only white of egg and milk as the test meal, and in most cases to remove the stomach contents in two and a half hours, not in five.

The use of test meals is chiefly limited to intractable cases of functional disorder of the stomach, in order to decide exactly what function is deficient, or to see whether the diminution of the action of the stomach is permanent, as in cases of gastric catarrh. In ulcer, and in the majority of cases of cancer, the test meal is inapplicable. In the first case the sound must not be passed, and in the second place a test meal is unnecessary, as it is in the majority of cases of functional disorder. The stomach sound is not to be passed when there are any signs or symptoms of thoracic aneurysm; when there is a severe wasting disease, or one tending to syncope, such as advanced pulmonary tuberculosis or serious cardiac disease, when there has been recent bleeding from any part, or in cases of great debility, or in advanced age.

GASTRIC INDIGESTION.

By functional disorder of the stomach is meant the condition of indigestion of food which results from a change in the activities of the stomach. Indigestion of the food also occurs in organic disease of the organ; such as congestion, catarrh, new growth, or long-standing ulcer. In the class of cases now under consideration, there are no organic changes in the organ, or none of any permanent character.

Cases of functional indigestion may be divided into three classes. Although in all, food is the direct inciting cause of the disorder, yet in the first case, which I have elsewhere called *gastric irritation*, food plays a very large part in the etiology of the disorder. (2) In the second class of cases, which I have called *gastric insufficiency*, there is a primary functional defect in the stomach, usually resulting from some general disorder, such as anæmia, gout, or acute infective disease. (3) In the third class, which will be discussed under the heading of *nervous dyspepsia* or

neuroses of the stomach, the symptoms are mainly those referable to the nervous system.

All these classes of cases run into each other, and may at one time or another present symptoms which are very similar. A distinction can, however, be made in the majority of instances from the history of the patient, the general condition present, or from the results of treatment.

Many different classifications have been made of dyspepsia, such as acid dyspepsia, atonic dyspepsia, flatulent dyspepsia, and so on. These, however, appear to me very unpractical divisions, and the classification I have used has been of great service to myself personally, both in the recognition and in the treatment of functional disorder of the stomach.

GASTRIC IRRITATION.

In gastric irritation the symptoms and the examination of the process of digestion in the stomach show the results of irritation, in which not only the secretion of the gastric juice is affected, but also the motor activity of the organ, the blood supply during digestion, and the innervation.

Etiology.—Under the heading of gastric irritation comes by far the largest number of cases of functional disorder of the organ; and what may be considered as nervous dyspepsia is really only part of gastric irritation with a prominence of nervous symptoms. It includes those cases which are usually described as acid dyspepsia. It is usually primary, but it may be associated with certain diseases or general conditions of the body. As a functional disorder it may last a considerable time, even years, and one of its features is that there are periods of quiescence, during which digestion is fairly well performed, and periods of exacerbation, in which the symptoms of dyspepsia are almost intolerable. It may, however, lead to gastric catarrh, inasmuch as the repeated irritation, which produces functional disorder, not infrequently leads to inflammation.

Age and Sex.—It may occur at any age: in the infant, whether fed by the wet nurse or by the bottle, in the child, in adult life, and in old age. Sex has but little influence, except that in adult life the more direct cause of the condition is, in women, excessive tea-drinking, and in men, excess of food, as well as of food accessories, especially alcohol.

Temperament.—Those who may be described as of a nervous temperament are especially prone to gastric irritation; such individuals being particularly affected by periods of worry, anxiety, or excitement.

Heredity plays a more important part in nervous dyspepsia than it does in simple gastric irritation.

Climate and race have no influence, except as regards the character of the food eaten. The most important factor in the etiology of gastric irritation concerns the food and the mode of living of the individual. For a healthy existence a sufficiency of food and of exercise and a congenial occupation are necessary. Insufficiency of food, even with much exercise, leads to the disorder. More frequently, however, an insufficiency of exercise is the cause, leading, as it does very frequently, to the eating of a large quantity of food at meals, and the taking of unsuitable quantities of alcohol and tea. Thus the disorder is met with as frequently among the well-to-do, or the professional classes, who lead sedentary lives, as amongst the poor, as for example the sempstress who works ten hours a day in a badly ventilated room. With regard to food, the arrangement of meals is of importance. A large meal ought to be followed by a period of bodily

rest and recreation (not sleep), and should not be succeeded by another large meal within five hours. Meals eaten hurriedly lead to gastric irritation, as also does work, mental or bodily, directly after a heavy meal. Large meals eaten before going to sleep are a factor also.

An important factor to be considered is imperfect mastication, which may be either due to toughness of the food, to the habit of rapid eating and bolting of the food, to pain caused by decayed teeth, or to the absence of teeth. The stomach cannot for long cope with unmasticated food. The bulk, composition, and reaction of food are also important. Excess of food, as has been stated, gives the stomach no rest, and from its mere bulk it produces disorder by throwing too much work on the stomach, so that during the day the stomach is never empty; and although there may be at first hypersecretion of the organ to enable the food to digest, finally the secretion becomes deficient with repeated large meals, and the movements of the organ inefficient.

As regards the composition of the food, a certain amount of proteids, carbohydrates, fats, salts, and water, are necessary in the daily diet in order to maintain nutrition. In the dietary of the well-to-do an excess of meat is a frequent cause of gastric irritation; in that of the poorer classes, an excess of vegetable food has the same effect. A large amount of meat leads to hyperacidity of the stomach contents, which is partly due to an excessive secretion of hydrochloric acid, and partly to the liberation of sarcolactic acid contained in the meat. A large amount of meat, therefore, leads to excessive secretion of gastric juice, and this, in time, to disorder. On the other hand, an excessive amount of vegetable food, which is not digested in the stomach, irritates the organ from its mere bulk, and more especially since such food frequently contains an excess of organic acids and salts, which increase the acidity, as well as a certain amount of cellulose, which is not digested in any part of the stomach or intestines. The amount of cellulose contained in different food-stuffs varies, *e.g.* fine wheaten flour contains 0.29 per cent. by weight; and whole-meal flour, 1.9 per cent.; barley and rice flour, about 0.5 per cent.; potatoes, 0.69 per cent.; spinach and cauliflower, about 1 per cent.; and fine oatmeal contains as much as 1.86 per cent.

As regards the chemical reaction of food, all that need be said is that food must not be taken too acid. The cooking of food is important as regards its digestibility. Bad cooking of food is a frequent cause of gastric irritation, either by making the food tough, or by destroying the flavours which are developed during good cooking; or, as in the case of starch, by not loosening the grains of which the starch is composed. Of as much importance in the production of gastric irritation as food, are the food accessories, such as alcoholic drinks, tea, and coffee. To some extent these accessories are useful in digestion; taken in excess, however, they act as irritants, their action in this respect being slow and extended over a long period of time. Alcoholic drinks, especially beer, port, sherry, hock, burgundy, and claret, delay the chemical processes of digestion, and lead to an increased organic acidity of the stomach contents. Alcohol itself, taken with the meal, has this action, though in moderate quantities the action is not without benefit, since the process of digestion is slow at first, and thus more perfectly performed; and later on the alcohol stimulates the secretion of gastric juice, and thus helps the digestion of a large meal. The taking of alcoholic drinks does less harm when taken with meals than when taken on an empty stomach; but they may cause bad effects in some individuals, even when taken in moderate quantities.

The final result of an excess of food or of food accessories on the stomach, is to cause the delay of food in the stomach by affecting the movements of the organ, as well as to cause the hypersecretion of hydrochloric acid which leads to definite symptoms.

Relation to other diseases.—Gastric irritation may be present in cancer of the stomach, as well as in infective disorders, such as tuberculosis, chronic malaria, and in convalescence from typhoid fever, scarlet fever, measles, rheumatic fever, and influenza. Its presence in these conditions is frequently preceded by some effect on the stomach, altering its functions, which brings it into relation with the cases of gastric insufficiency.

Pathology.—The pathological conditions present in gastric irritation are not associated for a very long period with any organic changes in the glands or in the muscular coats of the organ. They may be divided—(1) into the condition of acidity of the stomach contents; (2) into the condition of the movements; and (3) into the condition of digestion.

1. In such cases there is a secretion of very acid gastric juice during digestion, and this may continue after digestion is completed; the organ may thus never be free from some acid liquid and remnants of food. Cases, however, differ, as in some a large amount of acid is secreted in an hour or an hour and a half from the time of taking the meal; and this continues during the process of digestion, ceasing towards the end. In other and more severe cases the secretion continues even after the mass of food has been expelled into the duodenum. The degree of acidity which has been found is far above the normal. It may be 0·3 or 0·32 per cent. (Reichmann), or even higher, the normal being 0·2 per cent. The examination of the stomach contents of 222 persons during fasting showed that they were acid, the acidity being due to hydrochloric acid in 179 or 81 per cent. (Jaworski). The continued irritation of the stomach by an excess of acid causes an increased secretion of mucus, at any rate in the early stages of the disorder. This, however, is not a feature of gastric irritation, as it is in gastric catarrh.

2. The movements of the stomach are at first excited in gastric irritation chiefly by the excess of food, as well as by the hyperacidity; so that the increased activity leads to more rapid digestion of food. This may be so well marked that the food is too rapidly expelled from the organ, leading to great distress. In other cases there is well-marked spasmodic contraction of the stomach, which occurs, particularly, when irritant articles of diet are taken; a spasm, which is only relieved by the expulsion of the contents of the organ through the duodenum or by way of the gullet. In not a few instances, however, gastric irritation is associated with atony of the organ and some degree of dilatation.

3. The congestion which occurs in gastric irritation is a temporary condition, being, like the hyperacidity, an exaggeration of the normal condition of the organ during digestion. Its continuance renders the stomach more sensitive; in many cases it is directly associated with the pain experienced during digestion.

Symptoms.—The mode of onset of gastric irritation is not commonly acute; it is usually insidious, the symptoms being very gradual in their onset, at first being caused by repeated slight indiscretions in diet or irregularity in the mode of living. In its course, gastric irritation is charterised by periods of only slight disorder, intervening on other periods of more or less acute exacerbation.

Acute gastric irritation occurs usually as the result of large meals or

of irritating food. It is frequently referred to euphemistically as a "bilious attack," whereas in reality it is a food debauch affecting the stomach. The symptoms which occur in such cases are not developed during the partaking of a meal, nor for perhaps two hours or more afterwards; then a sense of fulness and discomfort is experienced in the epigastrium, accompanied by nausea, and frequently terminating in the ejection of the whole of the contents of the organ, which gives relief. The vomited matters are hyperacid, the acidity being due to an excess of hydrochloric acid. During the day following this occurrence the appetite is lost, and frequently loose motions are passed. Acute dilatation of the organ may result from a single large meal, but in these cases there is some chronic disease already present.

The physical signs which are present in acute gastric irritation show that the stomach is firmly contracted, its contents being felt as a round ball in the epigastrium. There is little or no tenderness, but manipulation may cause eructation of gas, or even vomiting. There is a thickly-coated tongue, with a lingering, nauseous taste in the mouth, lassitude, and frequently headache, while the complexion is pale.

Chronic irritation.—Chronic irritation is the more common disorder, and comprises by far the larger proportion of cases of functional disorder of the stomach. The symptoms which are observed, and which, as a rule, preserve their individual features in each particular case, may be divided into those which are general and those referable to the stomach. The latter are shown in a sense of fulness, weight, and oppression in the chest after eating, as well as pain in the back and over the angles of the scapulæ. The more general symptoms are referable to the nervous system, such as headache, palpitation, drowsiness, mental depression, sleeplessness, vertigo, hiccough. The symptoms referable to the stomach always appear in relation to the food, coming on at various times after the meal, and are most marked after the principal meal of the day, or in the evening when the stomach has had the three daily meals to digest.

The sense of weight, fulness, and oppression in the epigastric region may come on directly after eating, but is often delayed for half an hour, or for one or two hours, and it may then last until the next meal, which relieves it. Pain in the chest and between the shoulders bears a similar relation to the meal. The delayed onset of the pain after the meal is due to the fact that at that time the stomach has secreted an amount of excessively acid gastric juice, sufficient to irritate the mucous membrane. The continuance of the pain for long periods is ascribable to the delay of food in the organ, although this is not always the case, since the stomach may be rapidly emptied by an over-excitable muscular coat, and the symptoms continue as the result of continued secretion of hyperacid gastric juice. After a time these sensations are more or less continuous, the stomach, in fact, being never at any time empty.

Flatulence is a frequent symptom in gastric irritation. It is not due to bacterial fermentation of the food, but may be caused by one or other of the following conditions:—

It may be due to the accumulation of small quantities of gas, chiefly carbonic acid, which are generated from time to time in the stomach and small intestine, and which are not propelled onwards in the normal manner, but are eructated. This form of flatulence is common in the middle-aged and the old.

Flatulence may be due to swallowed air, or to swallowed saliva, the

carbonates of which are decomposed by the acids of the gastric juice, setting free carbonic acid.

It may be due to the regurgitation of pancreatic juice into the stomach, the carbonates of which are decomposed, setting free carbonic acid. This occurs in flaccidity of the stomach walls with patency of the pylorus. In some cases it has been supposed that large quantities of gas may be discharged from the blood into the stomach and intestines, and then be eructated.

Vomiting is a frequent symptom in the acute exacerbations of chronic gastric irritation; the vomiting is in this case directly due to the presence of irritating food in the stomach, as well as to the excessive secretion of hydrochloric acid, and occurs more commonly in patients with excitable nervous systems, or in the anæmic. In some cases, vomiting may occur after every meal; sometimes directly after a meal, sometimes not for one or two hours. It may also occur in the morning, in cases where heavy suppers have been taken before going to bed. Vomiting is kept up by continued indiscretions in diet, and is cured by proper dieting. The vomited matters may, in some cases, contain a little mucus, but it consists chiefly of digesting food, and contains peptones. It is very acid, the acidity being due mainly to hydrochloric acid, which is usually present to an amount of over 0·3 grm. per cent. This hyperacidity is sometimes absent. Active pepsin is always present.

Cases of gastric irritation may continue with the symptoms above described for many years, and may have omissions of greater or less duration, and exacerbations, which render the sufferer's life unendurable for a time, causing, in some cases, restlessness and mental inactivity during the day. By proper treatment, complete recovery is the rule; but, on the other hand, through neglect, permanent injury may be done, so that the digestion becomes impaired. Catarrh of the stomach may result, with a profound diminution in the functions of the organ; or permanent dilatation of the stomach may occur, with symptoms which will be discussed later.

The appetite may be normal or increased, and may even be voracious. Later on it becomes capricious, and long-continued gastric irritation leads to diminution of the appetite. The tongue is frequently coated, especially in the morning on waking, and there is a nasty taste in the mouth, which is clammy from mucus. Salivation frequently occurs from gastric irritation; usually after meals, at the time of greatest acidity for the stomach contents. In some cases, on the other hand, chiefly of long duration, there is a greatly deficient secretion of saliva, so that the mouth is always dry (xerostomia), which adds greatly to the distress of the patient. Constipation is the rule in gastric irritation; the bowels being opened once in one or two days, or sometimes not for a week, or only with medicine. Frequently, however, there is an alternating condition of constipation and diarrhœa; there being one or two days of looseness of the bowels, followed by constipation. Lienteric diarrhœa may also occur, coming on directly after, or soon after, a meal. This condition appears to be associated with irritability of the muscular coat, whereby the food is rapidly discharged into the small intestine.

The chief changes that occur in the urine are a tendency to alkalinity, a diminution in the quantity of urine secreted, and an excessive excretion of phosphates. Albuminuria is rarely present; but albumoses may be found in the urine.

Effect on general nutrition.—As a rule the patients subject to this

disorder do not waste, at any rate for some time; but this is explained by the fact that there is more than sufficient hydrochloric acid and pepsin to digest the food in the stomach, and the small intestine is normal; but long-continued gastric irritation leads to pallor, flabbiness of the muscles, and to increased myotatic irritability. When wasting occurs, it is naturally associated with some dilatation of the organ, or with prolonged diarrhœa. The loss of flesh, however, is not progressive. The course of the disease goes from bad to worse, rendering the patient's life utterly miserable, if it be not treated. Patients are very apt, during the periods of relief from symptoms, to commit indiscretions in diet, which bring on another attack, and so keep up the disorder. There is, however, no disease which is more amenable to treatment in its early stages. The results of untreated gastric irritation are gastric catarrh and permanent dilatation of the organ.

Diagnosis, treatment.—These are considered under Neuroses and Catarrh.

GASTRIC INSUFFICIENCY.

Gastric insufficiency is a condition in which the functions of the stomach are diminished. In prolonged gastric irritation this is the case. It is also the case in catarrh and in cancer of the organ.

Etiology.—The term "insufficiency" is applied more to those cases in which the disorder of the organ follows, or is associated with certain diseases; and from a practical point of view, this distinction from gastric irritation is of some importance. The symptoms are directly brought out by the presence of food in the organ; yet irritation is not the direct cause of the primary condition of the stomach, as in gastric irritation. The general depression of functions which occurs in those who lead a sedentary life, with much mental work, affects the stomach, leading to deficient activity; and this occurs more readily towards the middle period of life in both men and women. In old age the functions are diminished generally, and a smaller amount of food is taken than in the vigorous period of life. In women, at the menopause, extreme insufficiency is frequently observed, as well as in prolonged lactation. In young adults, however, some recognisable morbid condition of the body is present. These may be divided into two classes. Non-febrile conditions, such as continued hæmorrhage, from whatever cause, whether rectal or uterine; prolonged suppuration, as well as syphilis and tuberculosis; and all the conditions which lead to anæmia predispose to or actually induce gastric insufficiency.

A state of fever diminishes the activity of the stomach, and during convalescence the return of function is usually slow. Indiscretions in diet at this period may lead to chronic gastric disturbances, shown chiefly by dilatation (deficient motor activity), or by a deficiency of the chemical processes of digestion. It is observed after typhoid fever, scarlet fever, rheumatic fever, measles, and influenza, and is a frequent accompaniment of progressing pulmonary tuberculosis.

Clinically, gastric insufficiency may perhaps be divided into cases which are temporary, and those which are permanent, the permanent cases being due to organic changes in the walls of the stomach, whether atrophy, inflammation, or new growth.

Pathology.—In gastric irritation, in response to the stimulus of food, there is a deficient secretion of the gastric juice and deficient motor activity, both functions failing before the meal is digested. This leads to

great delay of the food in the organ, and subsequent dilatation. The food which remains may undergo bacterial fermentation, although this is not common.

Symptoms.—The symptoms which are observed in gastric insufficiency are induced by the food which is taken, and food acts as a constant irritant to the organ. They come on directly after a meal, and if continued large meals are taken, they last the whole day through, and sometimes during the night. There is usually a sense of epigastric fulness and of oppression on the chest, which may be associated with dyspnœa. Flatulence is a constant symptom, and is as a rule due to one or other of the causes mentioned under gastric irritation (p. 654). It is usually associated, however, with moderate dilatation of the organ. Acid eructations do not usually occur, and vomiting is not a symptom.

Reflex symptoms are extremely common in gastric insufficiency, and are chiefly nervous, due partly to the excitability of the nervous system, and partly to the condition of anæmia present. Reflex pain is common, as well as tenderness, most frequently in the lower part of the left axilla. This localised pain is almost always associated with flatulence. Headache is common, as well as drowsiness after meals, sleeplessness, lassitude, disinclination to exertion; mental inaptitude and apathy, and a melancholy view of life. The face is often pale and anxious-looking; the complexion may be muddy. The appetite is always diminished, and the tongue is broad, pale, flabby, and tooth-indented, but is not usually coated. Constipation is the rule. In gastric irritation, looseness of the bowels may be present, owing to the irritation of scybala in the colon. The pulse is feeble, not very frequent, but regular. The effect on general nutrition of gastric insufficiency is more marked than in the case of gastric irritation. Wasting is very common, or, if wasting is not present, the muscles are very flabby, and may show myotatic irritability. Gastric insufficiency may be a permanent condition in old age, or in those who have inherited a weak digestion. When it occurs in febrile disorders, it is highly amenable to treatment, but if neglected, leads to great dilatation of the organ.

Diagnosis, treatment.—These are considered in the following section.

NERVOUS DYSPEPSIA.

The cases which may be included under this heading are those in which, while there are stomach symptoms of greater or less variety, there is a special prominence of symptoms referable to the nervous system. These nervous symptoms belong to two categories — in one, the prominent symptoms are referred to the stomach region; in the other, they are reflex, and may aptly be called "gastric reflexes."

Etiology.—Nervous dyspepsia occurs more particularly in those who possess what is called a nervous temperament; to speak more accurately, in those in which a slight stimulus produces a large response from the central nervous system; so that in these cases there is an over-excitability of the central nervous system. The stomach, as has been said, is connected to the central nervous system by means of the vagus nerves, and by the sympathetic nerves which come from the dorsal region. The vagus contains two sets of fibres, both afferent and efferent, and although its direct influence on the functions of the stomach in health is not very profound, yet it may be considered as the chief conductor of impulses in those cases of disease in which symptoms referable to the nervous system are pro-

minent.   There is not only an increased excitability of the central nervous
system in these cases, but also irritability of the nerve-endings in the
stomach.   Nervous dyspepsia may indeed be considered as one of the mani-
festations of the nervous conditions which are described as hysteria or
neurasthenia, and hypochondriasis.

Pathology.—The condition of the stomach in nervous dyspepeia is a
very variable one, both as regards the secretion of gastric juice and the
motor activity of the organ.   Variability constitutes one of the most im-
portant points in diagnosis.   Thus in an individual case there may be at
one time an excessive secretion of hydrochloric acid, and at another a
diminished secretion; in another case the chief change may be one of
deficient motor activity, showing itself in more or less dilatation of the
organ, as well as, at intervals, irritability.   At one time in such patients the
processes of digestion may be exceedingly good, at another greatly deficient.

Symptoms.—Symptoms referable to the nervous system may be
present in ordinary cases of gastric irritation or gastric insufficiency, such,
for example, as an affection of the appetite, the occurrence of thirst or
xerostomia, the occurrence of reflex pain or of pain in the epigastrium,
palpitation, cough and dyspnœa, tingling and numbness, impaired vision,
buzzing in the ears, drowsiness, sleeplessness, nightmare, vertigo or
hiccough, inability to do mental work, and the dread of a fatal seizure,
cardiac or apoplectic.   Similar symptoms are present in cases of nervous
dyspepsia; but their characteristic in this condition is their great ex-
aggeration.

Practically, the cases may be divided into two classes—first, cases of
gastric irritation, with prominence of one or more nervous symptoms; and
second, cases in which the digestion is normal as regards the chemical
processes, but there are nervous symptoms, either general or related to the
stomach.

With regard to the cases in which there is exeggeration of the reflex
nervous symptoms which occur in cases of gastric irritation, nothing need
further be said.   But a few remarks are necessary on the exaggeration of
the symptoms referable to the stomach, which occur in neuroses of the
organ.   The first is *pain.*   Such cases are frequently referred to as
gastralgia.   In this condition pain may be extremely severe, neuralgic or
shooting in character, rarely dull and heavy, and showing a tendency to
disappear suddenly.   In some cases pain occurs chiefly before food is taken,
food relieving it; in others, and this is more important from a diagnostic
point of view, the pain, although more or less present between meals, is
exaggerated after a meal, is localised in the epigastrium, and is accom-
panied by acute and localised tenderness.   This localisation is sometimes
remarkably limited.   It may persist in the same situation during the
whole course of the illness, a condition which renders the diagnosis from
ulcer, in some cases, extremely difficult.   The absence of vomiting with
this localised pain is very distinctive of neuroses.   It is a noticeable fact
in these cases, also, that the local pain and tenderness is not so greatly
affected by the character of the food, whether solid or liquid, as in cases of
ulcer of the stomach.   Frequently also there are associated abdominal
neuralgic pains, sometimes referred to the colon, and sometimes to the
small intestine.

Eructatio nervosa is a condition which frequently occurs in nervous
dyspepsia, and is the persistent and repeated eructation of gas or of small
quantities of liquid from the stomach.   The eructated liquids may show

that the process of digestion is normal; the liquid may also be neutral or even alkaline, and in some cases it is no doubt swallowed saliva. The condition is dependent on irritability of the stomach, which causes slight eructations. Associated with this condition, but more frequently existing by itself, is the excessive flatulence from which those patients suffer; a flatulence which may be described as enormous, coming on at irregular intervals, and frequently suddenly; occurring also towards the end of the day, and rendering the patient utterly unable to perform any exertion, mental or bodily. The origin of the gas in this condition is partly swallowed air and partly, it is supposed, transudation from the blood. The disappearance of the flatulence may be as sudden as its onset.

Hiccough is a prominent symptom in individual cases, and is usually associated with the presence of irritating food in the stomach. Its onset and disappearance may both be quite sudden.

Vomitus nervosa is a symptom commonly observed in women. It usually occurs after meals, is associated with well-marked constipation, and frequently with very few symptoms of indigestion of food. The vomiting is sudden, and consists almost solely of the normal contents of the stomach, and may persist with slight periods of intermission for years.

Nervous dyspepsia occurs chiefly in young adults, and in females above the age of puberty, and is characterised by the symptoms previously mentioned, by a variable appetite, and by the fact that the chemical processes of digestion are found to be practically normal. There may be a moderate dilatation of the organ at one time or other in the course of the illness.

The course is usually a very characteristic one; inasmuch as a patient suffering severely from gastralgia or flatulence for a period, say of a month, will have a complete and sudden intermission of the symptoms. Such a patient feels during the attack unfit for any occupation; during the intermission he may feel perfectly well. Such an occurrence as this in the course of a case indicates clearly its nervous origin.

Such an abrupt intermission does not occur in those cases of nervous dyspepsia which present the peculiarity of being able to take but little food, even the simplest diet; even milk causes discomfort, solid food being absolutely intolerable. These patients may remain in this condition for months, may waste considerably, and be unfit to follow any occupation. In these cases the stomach appears simply to have struck work, there being no sign of any organic disease of the mucous membrane. As a rule it is an intractable condition, though some patients may improve considerably under treatment. Improvement, to some extent, is the rule in cases of nervous dyspepsia; relapses, however, are extremely common. Although temporary relief can be given, no permanent cure is made in severe cases.

Diagnosis.—The question of the diagnosis of functional from organic disease of the stomach frequently arises in individual cases, and may present great difficulty for a time. This is more especially the case in the diagnosis of neuroses of the stomach from ulcer of that organ, in the diagnosis of gastric catarrh from nervous dyspepsia and gastric insufficiency, and in that of cancer from gastric insufficiency. Some of the points in the diagnosis will be considered under the headings of Catarrh, Ulcer, and Cancer.

Ulcer.—Cases both of gastric irritation and of nervous dyspepsia may, with difficulty, be distinguished from ulcer, and there are not a

few cases of ulcer of the stomach which present the features of gastric irritation, and only declare themselves as ulcer after some time by an attack of hæmatemesis. In the diagnosis between gastric irritation and ulcer the points to be looked to are the character of the pain and of the vomiting, and the course of the disease. Both may occur in young women; in ulcer the pain is localised in the epigastrium, and is associated with localised tenderness, both pain and tenderness being dependent on the ingestion of food, and relieved by vomiting. Vomiting is frequent, especially in the continued taking of unsuitable diet, and repeated vomiting may lead to some amount of wasting. Hæmatemesis may or may not be present.

Gastric irritation, on the other hand, presents during its course quite different features. Although there may be times at which nausea and vomiting occur after food, for a duration of, perhaps, two or three months, yet the vomiting is not a serious or frequent symptom, and is very readily controlled by treatment. Indeed, it ceases without any definite medical treatment, because such patients find, unlike those suffering from ulcer, that certain foods can be taken with least distress, and so gradually confine themselves to a more or less suitable diet. Vomiting is more frequent in women than in men in gastric irritation. The pain in gastric irritation is not continuously epigastric, nor is it associated with localised tenderness. When epigastric pain is present it is usually transient, being produced by some definite indiscretion in diet. Epigastric pain in gastric irritation, however, may go through to the back, as in ulcer; and if frequent vomiting is present, there may be a diffused tenderness over the stomach; but all these symptoms may be rapidly relieved within the course of a week by appropriate treatment, much more rapidly than in cases of ulcer.

Nervous dyspepsia gives rise to more difficulty in the diagnosis. It is a disease, like ulcer, most common in young women over the age of puberty. One of the main distinctions of cases of nervous dyspepsia from those of ulcer lies in the fact that they present extremely variable and changing symptoms. There are cases of what may be called localised gastralgia, both in men and women, which are frequently diagnosed as ulcer. In these there is pain after food, often excruciating, and localised to one spot in the epigastrium; and the only point in which such pain and tenderness differs from that which occurs in ulcer is, that it is shooting and very severe. Thus, as regards the local tenderness, a slight pressure on the tender spot may call forth agonies of pain, an occurrence which is sometimes observed in cases of ulcer; and this localised tenderness in nervous dyspepsia may last for years, unless appropriate treatment is adopted. In most cases it differs widely from the similar pain in ulcer by the absence of vomiting. Other cases of nervous dyspepsia which simulate ulcer are those in which there is repeated vomiting, which may occur after every meal in the day, is usually associated with epigastric pain, and may continue for many months. It is correctly described as *vomitus nervosa*, and is associated with other manifestations of an excitable nervous system, such as referred pains, headache, neuralgia, and dysmenorrhœa.

Broadly speaking, one looks for the distinction between nervous dyspepsia and ulcer in the fact (1) that in nervous dyspepsia the symptoms frequently cease suddenly for a week or so, without any obvious change being made in the diet or treatment; and (2) that if such patients are placed under strict dieting for about a fortnight, they do not improve so decidedly or so readily as those suffering from ulcer.

Gastric catarrh.—The symptoms of chronic gastric irritation and of chronic catarrh bear a close superficial resemblance, but they are essentially two different diseases, since one is purely functional and the other is a chronic inflammatory process. Gastric irritation may, of course, pass into catarrh, and continued irritation leads to chronic inflammation; but there are many cases in which this is not so. Both are essentially chronic affections, with a tendency to have more or less acute exacerbations. Epigastric pain, which is only a transient symptom in gastric irritation, is frequent, and often severe, in chronic gastric catarrh. It is commonly diffuse, and associated with one or more areas of epigastric tenderness, varying in size. Vomiting is present in both affections, and in catarrh is more closely associated with diffuse epigastric pain than in gastric irritation. The vomited matters in gastric irritation are usually hyperacid, and consist of the digesting food, with no mucus. In chronic catarrh, on the other hand, the vomiting is never hyperacid, the food is but slightly digested, and there is an excess of mucus present. Moreover, in catarrh there is a greater dilatation of the stomach than in chronic gastric irritation. In gastric catarrh, hæmatemesis, although not common, may occur, and is always slight; in gastric irritation it does not occur at all.

In some of these cases, the employment of a test meal is of great service in the diagnosis of the condition. It is not uncommon for cases of nervous dyspepsia to be diagnosed as catarrh, and indeed catarrh or gastritis is frequently diagnosed in cases which are purely functional. This is an important point, inasmuch as catarrh of the stomach is a very serious disease; while functional disorder is comparatively unimportant, or, at any rate, it is an affection which is readily amenable to treatment. The attacks of epigastric pain and vomiting, occasionally with a little mucus, which occur in some cases of nervous dyspepsia, may lead to the suspicion of catarrh of the organ; but if the case is watched, it is found that these symptoms soon subside when a suitable diet is ordered, and that the presence of mucus is not constant. Moreover, and this is the chief point, the amount of free hydrochloric acid which is present in the digesting gastric contents is not only not below, but is more frequently above, normal —0·3 grm. per cent. or over.

Functional gastric insufficiency cannot be mistaken for catarrh, inasmuch as the history shows some definite cause, whether acute disease or not, for the affection of the stomach; and there is an absence of epigastric pain and of vomiting, with usually a large amount of flatulence and a moderate degree of dilatation of the organ, these symptoms being greatly relieved by treatment. In cases, however, of atrophy of the glands of the organ, by no means common, the condition is, as a rule, secondary to catarrh, and presents many features of what has been called "permanent gastric insufficiency." There is, however, in many of these cases epigastric pain; vomiting is not common, although nausea may be present. Flatulence is a feature, and wasting is frequently observed.

Cancer.—The diagnosis of cancer from functional disease is more appropriately considered under the heading devoted to it. It may, however, here be said that in the early stages of cancer of the stomach there are indefinite symptoms of indigestion of food occurring in the course of the day; there may be no specific symptoms pointing to cancer. The points, however, which are to be attended to are the continuance of the symptoms during a definite period, and without any history of a definite cause, asso-

ciated with a progressive wasting and loss of appetite, and, it may be, cachexia.

Treatment.—The treatment of functional disorders of the stomach is both medicinal and dietetic, as well as hygienic. Massage, electricity, and washing out of the stomach are also of benefit in some cases. Without dietetic treatment drugs are of little avail, although these are essential, especially in the treatment of the disorders in their aggravated form. The conditions which have to be treated in functional disorders are—(1) alterations in the secretions of gastric juice, either hyperacidity, due to hydrochloric acid, or deficient acidity, due to the diminution in the secretion of the hydrochloric acid—sometimes there is a diminution in the amount of pepsin; (2) alterations in the motor activity of the stomach, chiefly a diminished motor activity (myasthenia or atony of the organ), or occasionally irritability or spasmodic contraction; (3) a varying degree of hyperexcitability of the nerves, accompanied in many cases, no doubt, by a persistence of the digestive congestion of the organ, these conditions being shown by discomfort and pain.

The restoration of the functions of the organ, when disordered, is a matter of time and treatment, and frequently symptoms have to be treated immediately, such as pain, vomiting, flatulence, and excessive acidity. The remedies which are used in treatment act as antacids, as stimulants of secretion, as stimulants to the motor activity, as sedatives, both for the increased secretion of gastric juice and for nervous and motor irritability; and in some cases remedies supply an insufficiency in the secretion of hydrochloric acid or pepsin. It cannot be too strongly laid down that anything like powerful remedies in the treatment of functional disorder of the stomach is out of place, and does more harm than good.

In the dietetic treatment of functional disorder, the objects to be borne in mind are (1) to give the patient during the day only as much food as the stomach can digest with the least discomfort; (2) to remove irritants from the diet. With all these conditions, there is delay of food in the organ, and in some cases the stomach contents are always acid, irritating the organ; in others, digestion seems to cease with the stoppage of the secretion of gastric juice. In all cases the amount of food taken in health is to be reduced in quantity, and altered in character, either because of the pain produced, or of vomiting, or of irritability of the organ. The irritating substances in the diet which do harm in the disordered stomach are too large a quantity of organic acids or salts, such as exists in beef, beef-tea, many vegetable foods, and fruits; an excessive amount of carbohydrates, more particularly starch, and all fats; and, lastly, a large amount of cellulose. All food accessories are irritants, or tend to become irritants, in gastric disorder; and indeed some, such as tea and alcoholic drinks, are in many cases the chief factors in producing gastric irritation. In the treatment of all aggravated forms of functional disorder, food accessories have to be removed from the dietary—all alcoholic drinks, strong tea, and strong coffee more particularly.

Of great importance in the treatment of functional disorder is the regulation of the mode of life, more particularly for the prevention of the recurrence of attacks than for the immediate treatment of subacute attacks. Regular and digestible meals, regular hours, and regular pleasurable exercise are the three chief factors in the treatment of such patients between their attacks. Not more than three meals are to be taken in the day, with, as a rule, nothing between them. The largest meal is to be in

the middle of the day, and after each meal there ought to be a period of half an hour at least for rest and recreation. In many cases, too, attention to the teeth is of the highest importance, inasmuch as the disordered digestion may depend to a very great extent on deficiency of the teeth, or other conditions preventing proper mastication.

Gastric irritation.—Cases of gastric irritation come under treatment at various stages of the disease; usually, however, in one of the subacute attacks, and with a history of recurrent attacks for perhaps years past. Many of these patients find that particular articles of diet disagree with them, and gradually omit them, so that they improve for a time, relapsing again when they commit dietetic indiscretions.

The first class of cases to be considered are those in which there is great discomfort after food, with referred pains in the chest, with irregular vomiting of a very acid fluid, and with flatulence. Such patients have hypersecretion of hydrochloric acid, as well as hyperæsthæsia of the organ. They have to be treated medicinally by means of alkalies and sedatives. The alkalies to be used are:—Bicarbonate of sodium, 10 to 20 grs.; prepared chalk, 5 to 10 grs.; magnesium carbonate, 5 to 10 grs. Trousseau's antacid powder, which is an excellent preparation, consists of—bicarbonate of sodium, 5 grs.; prepared chalk, 10 grs.; magnesium carbonate, 5 grs. One powder is to be taken after each principal meal, and before going to bed. Alkalies may be administered, either before or after meals. Administered before meals in hyperacidity of the gastric contents, they neutralise the acidity of the liquid, thus preparing the stomach for the next meal; and, by means of the carbonic acid which is developed, they aid the organ in expelling its contents. Alkalies are given after meals, if the period of discomfort in digestion usually occurs one to two hours after a meal. They ought then to be given just before the patient becomes uncomfortable, and are useful this way in neutralising hyperacidity.

Alkalies are very useful, combined with sedatives. Mild sedatives which may be used in gastric disorder, are bromide of potassium (5- to 10-gr. doses) and iodide of potassium (2-gr. doses). The three most useful, however, are cocaine hydrochlorate, in doses of from one-fifth to one-tenth of a grain; dilute hydrocyanic acid, in doses of 3 minims; liquor morphinæ hydrochloratis, in doses of 5 to 10 minims. Carbolic acid in 5- to 10-minim doses of the glycerinum, ether and chloroform in the form of spiritus, and bismuth in the form of carbonate, are all mild sedatives; bismuth also acting somewhat as an antacid.

In the actual treatment, it is usually best to begin with an alkaline mixture, containing 15 gr. of bicarbonate of sodium, 3 minims of dilute hydrocyanic acid, 5 minims of spirits of ether, and an ounce of infusion of gentian, to be taken before the mid-day and evening meal, and again on going to bed. If there is much discomfort, morphine may be added to this mixture. It has the disadvantage, however, of increasing the constipation. The same mixture may be given after meals, and in the conditions which have been already mentioned. This mixture is extremely serviceable for warding off the attacks of indigestion, to which the patient is liable for many months after the acute attack has been treated. It may be taken for a long time without doing any harm. Antispasmodic remedies may have to be given, of which the most serviceable are spirits of ether and sal volatile, in doses of 15 to 30 minims, or cajeput oil in doses of 1 to 3 minims. Hot water, not more than a wine-glassful, frequently acts very well

as an antispasmodic. In such cases the administration of pepsin and other digestive ferments is of no avail, since there is no diminution of pepsin in the gastric juice. The exhibition of acids before meals is often useful, as they have a tendency towards diminishing the hypersecretion of acids. The administration of acids sometimes does harm, and many patients show great intolerance in respect of them. The antiseptic remedies so frequently given are of little use, there being no bacterial fermentation to counteract. The diet has to be carefully regulated, first, by cutting off all alcoholic drinks, and strong tea and coffee; by disallowing green vegetables, fruit, and frequently potatoes; and allowing only white bread, or toast made from white bread.

If the symptoms are severe, the patient had better be placed on a sterilised milk diet, at any rate for a few days; and then a graduated diet may be begun by means of bread and milk, Benger's food and milk, or the white of an egg beaten up with milk. This diet must be adhered to for breakfast and for the evening meal; the mid-day meal consisting of boiled fish or chicken, or a grilled minced chop may be added, with a milk pudding or custard. All prepared foods, pastry, and jam are to be avoided. When the functions of the stomach are recovering, butter may be added to the dietary, and vegetables slowly, namely, spinach and green peas. In these cases any danger from the loss of vegetable food may be obviated, by giving the juice of half an orange or half a lemon in water twice a day with meals.

In long-continued gastric irritation, besides the symptoms which have been mentioned, patients may show at the commencement of treatment wasting, flabbiness of the muscles, and frequently increased myotatic irritability. Usually in these cases there is some dilatation of the organ, it may be only after the principal meal of the day. Besides careful dieting, which has been already discussed, it may be said that the administration of sedatives, such as morphine, for any length of time, has to be carefully watched, as the atony of the organ may be thereby increased.

A very useful method of treatment for such patients is to insist upon complete rest from work of all kinds, and active exercise; and to combine with this rest, massage of the abdomen, as well as of the body generally. Abdominal massage is to be chiefly over the stomach region, and to be practised from left to right, in the direction in which the contents of the organ are expelled. Constipation and diarrhœa have to be treated; the latter condition, unless lienteric, being usually caused by the constipation. The treatment of the lienteric diarrhœa in gastric irritation is that of the stomach disorder itself, *i.e.* dietetic, with the administration of alkalies and sedatives before meals. Constipation itself, which is often a troublesome symptom in these cases, is to be treated by an evening pill of aloes and belladonna, with, if necessary, an aperient saline in the morning, or a small injection.

Gastric insufficiency.—The treatment of gastric insufficiency has to be carried out on different lines to those of gastric irritation; inasmuch as not only is there a deficiency in the functions of the stomach, but the general nutrition is affected, sometimes profoundly so, as shown by wasting, general weakness, and anæmia. The general treatment is therefore of great importance—hygienic treatment, and the administration of tonics. The tonics which are most useful are quinine and iron; but these must be given in very small doses, not more than 1 to 2 grs. of sulphate of iron, and 1 to 2 grs. of sulphate of quinine. Other

treatment, which is useful in these conditions, is general massage. Abdominal massage is also of service in the treatment of the atony of the stomach, which is usually present. The treatment of the stomach condition itself is different from that of gastric irritation, inasmuch as acids are here of great service. Acids are usually administered in the form of dilute nitrohydrochloric acid, in doses of 7 to 15 minims, with tincture of nux vomica, 4 to 6 minims; or liquor strychninæ, 3 to 5 minims. Bitters have to be given with care in this condition, inasmuch as they are apt to irritate the organ. They are best withheld, a simple flavouring agent being added to the mixture. In some cases the use of pepsin in powder is beneficial, in doses of 5 to 10 grs. after meals, or it may be mixed with the acid mixture. Antispasmodics may be required for the flatulence. In gastric insufficiency it is not always advisable to completely withhold stimulants, and it is frequently of service to administer with meals twice a day two teaspoonfuls of brandy, with 3 minims of liquor strychninæ in an ounce of water.

Nervous dyspepsia.—This is a matter of extreme difficulty. Not only do individual cases present an infinite variety of aspect, but in most instances the effect of treatment is but slightly noticeable at first.

The dietetic treatment has to be regulated to suit the needs of individual cases. In those cases where vomiting is severe, or where there is much pain in the epigastrium, patients may require to be placed on a strict milk diet, at any rate for a time; and in some cases the withholding of all food by the mouth, and the adoption of rectal feeding, has a most beneficial effect. Patients with nervous dyspepsia frequently exhibit remarkable idiosyncrasies as regards diet, and the routine adoption of a milk diet in all cases is not to be recommended. The physician, therefore, has to feel his way in the dieting, in order to determine what articles of diet, whether solid or liquid, are most easily digested by the patient. In cases where vomiting is not a marked feature, and where—associated with epigastric distress —there is a large amount of flatulence and numerous referred pains, the dieting has to be conducted on the same lines, and mistakes are often made in keeping such patients exclusively on a milk diet. Frequently, too, such patients are taught to wash their stomachs out themselves, which they do at irregular intervals, without medical direction. This practice is one strongly to be condemned in nervous dyspepsia, inasmuch as washing out the stomach ought rarely to be resorted to, and then only to relieve great distress.

The medicinal treatment of nervous dyspepsia varies considerably, inasmuch as such patients show an idiosyncrasy towards drugs, similar to that they exhibit towards articles of food; some are intolerant of acids, others of alkalies, others of iron, others of quinine and of bitters. A particular case would alter, in this respect, while under treatment. Great care, therefore, is to be taken in the administration of drugs to these patients, in order not to further increase the mischief. They nearly all require a stomachic sedative in one of the forms previously discussed under Gastric Irritation. They do not require antiseptic remedies.

As regards the administration of acids or alkalies, the decision as to which should be used must be made from the facts previously mentioned, as regards the presence or absence of hyperacidity during digestion. In some cases, the ordinary digestive mixtures do more harm than good, and all that is required is a quinine and iron tonic, to be given after meals. If

the patients do not improve under this treatment, if they still have a large amount of distress and pain, if the flatulence is great, and if there is well-marked insomnia and wasting and flabbiness of the muscles, the only plan of treatment which is of service is complete rest in bed, with isolation and graduated diet, with employment of general massage and local massage of the abdomen. Rest and treatment generally should be continued for at least a month. Some of these patients completely recover, whilst with others relapses are extremely frequent; and these are brought on, not only by indiscretions in diet, but also by worry and unhealthy occupation.

GASTRITIS.

Gastritis is either acute or chronic, and is an inflammation of the mucous membrane of the stomach. Acute gastritis may be divided into three different classes—(1) simple, gastritis catarrhalis; (2) toxic, gastritis toxica, due to poisons; (3) infective, gastritis mycotica, due to bacterial infection. Chronic gastritis is usually called chronic gastric catarrh, and may occur as a sequel to the acute stage; it may, however, be chronic from the first.

ACUTE CATARRHAL GASTRITIS.

Etiology.—Gastric catarrh, or inflammation of the mucous membrane, is the result of irritation of the organ. The irritants which act in the production of catarrh are certain articles of diet, such as those which contain a large excess of cellulose, and especially food accessories, such as alcohol and tea. Teetotallers, however, are not exempt from the disease. A second factor in producing the disease is persistent hyperacidity of the gastric contents, such as is present in cases of gastric irritation, or is due to an excessive amount of organic acids and salts taken with the food, or to an excessive formation of organic acids (lactic, butyric, and acetic) by the bacterial fermentation of carbohydrates in the stomach. The delay of food in the stomach is a third factor which aids in the production of catarrh.

Although these conditions must be considered the direct inciting causes of inflammation—and in some cases they are the only factors—yet gastric catarrh is closely associated in its etiology, not only with other diseases of the stomach, but with certain general diseases. It has previously been stated that it may follow gastric irritation. It is sometimes associated with cancer of the organ; it is but rarely associated with ulcer, at any rate in the early stages of the ulceration.

As regards general diseases, it is predisposed to by such acute febrile diseases as tuberculosis, scarlet fever, measles, rickets, pyæmia and septic diseases, pneumonia, and typhoid fever. Although acute catarrh of the stomach may occur in the course of these diseases, it is usually in the convalescent stage that it is likely to arise; during this period, when the stomach is recovering from the diminution of function which occurs during the acute illness, dietetic indiscretions are the exciting cause, and may lead to inflammation. In chronic Bright's disease, catarrh of the stomach may be observed; in gout it may be present, although a functional disturbance is the more common.

Pathology.—In acute catarrh there is active congestion of the

mucous membrane, with transudation of liquid, and a large amount of interstitial infiltration of the tissues by leucocytes. The epithelial cells lining the membrane show an increase in the number of goblet cells which produce mucus. The cells also undergo proliferation, and are eventually cast off, to a greater or less extent, in the mucus and liquid which is exuded from the surface.

The most important change, however, which occurs in catarrh of the gastric mucous membrane affects the glands. The epithelium of these becomes swollen and granular, the nucleus being pushed to the side of the cell; the cell stains badly, the granules are not soluble in ether, but are soluble in dilute acids. This affection of the glands, which occurs in catarrh of other mucous membranes, such as those of the nose and of the bronchi, is of great importance in the stomach, inasmuch as the secretion of the glands is of prime importance in digestion. Besides the granular change in the cells, they may also undergo mucinoid degeneration, which has the same effect as the granular degeneration, namely destroying their function. Fatty degeneration of the cell may also be the final stage of a catarrhal condition. Granular and fatty degeneration are more common than the mucinoid, the fatty change being well marked in chronic catarrh of the organ. When the catarrh becomes chronic, the secretion of mucus is continuous, at any rate for some time, although, if a large area of the epithelium is destroyed, the secretion diminishes. The degeneration of the glands is well marked, and is referred to as parenchymatous degeneration. Associated with this degeneration, or in some cases constituting the chief change in the mucous membrane, is interstitial fibrosis. Pigmentation may also occur. In the majority of cases the morbid changes are limited to the mucous membrane (see " Cirrhosis of the Stomach," p. 685).

Catarrh affects chiefly, or at any rate primarily, the pyloric region of the stomach ; but in not a few cases it involves the whole of the mucous membrane, and the degeneration of the glands may be more marked in the cardiac region than in the pyloric. It is rare in chronic catarrh to find the whole of the mucous membrane affected by the change, although in the subacute cases, which occur in the course of tuberculosis and other febrile diseases, the change may be practically universal over the mucous membrane. The muscular coat is sometimes affected. There may be simple atrophy of the muscular cell, but both fatty and colloid degeneration have been described.

The condition of *état mamelloné* is one of fibrosis of the pyloric region, associated with atrophy of the mucous membrane; the mucous membrane forming small projections or polypi. Microscopically, there is a small-celled infiltration, with the formation of connective tissue between the gland elements. In this condition, by the constriction of the mouth of the gland, cysts are formed, usually not large in size, but frequently quite visible to the naked eye. In one case of chronic catarrh, in which there was mucinoid degeneration, Langerhans found the mucous membrane formed into a sort of sponge by the numerous cysts which had developed.

The pathological condition which is present in gastric catarrh is that, during normal digestion, there is great interference with the necessary blood supply ; secondly, that there is a great diminution in the amount of hydrochloric acid secreted, to a less extent in the amount of pepsin. In acute cases hydrochloric acid and pepsin may be completely absent for a time. There is in the subacute and acute cases motor irritability of the

organ, and in more chronic cases there is a diminution of motor activity, and commonly dilatation. Absorptive processes are also greatly interfered with. The process of digestion is therefore greatly modified. In acute catarrh there is practically no digestion in the stomach; in mild chronic catarrh there is inability to digest an ordinary mixed meal, owing to the diminished function. Although some gastric juice is secreted in these cases, yet it is not sufficient to complete the digestion, and the organ is too weak to expel its contents. Delay of food therefore occurs, and this may be so marked, that ultimately bacterial fermentation ensues, leading to hyperacidity due to organic acids, and thus to a continued irritation of the organ.

Symptoms.—Acute catarrh is usually sudden in its onset, and is associated with either a food or a drink debauch. Frequently, in these cases, there is a predisposition to disordered digestion. The onset is characterised by vomiting and great epigastric pain. There is sometimes a slight rise of temperature, which is of but short duration. There is great prostration. The face is pale, sometimes drawn and sunken; the skin is cold and clammy, and may be covered with sweat. The pulse is frequent, regular, compressible. There are diffuse pains in the back and limbs; giddiness on exertion is sometimes a marked symptom. Delirium is not common. There is complete loss of appetite, accompanied by thirst and dryness of the mouth. Herpes labialis is not infrequent. The symptoms, therefore, of acute catarrh are those which are observed when an acute irritant poison is taken into the stomach, and, indeed, acute catarrh is caused by an irritant. The pain is burning, passes through to the back, and is accompanied by a sense of oppression on the chest. The epigastric pain is associated with deep tenderness, and frequently with rigidity of the muscles over the stomach region. Vomiting is a well-marked symptom, the vomited matters consisting at first of partly digested food, later on of food which shows no sign of digestion. The liquids removed from the stomach or vomited are slightly acid, neutral, and even alkaline. There is no free hydrochloric acid present. In the later stages organic acids may be present, due to bacterial fermentation; and an examination of the stomach contents frequently reveals the presence of bacteria in the mucus, even when no fermentation occurs. Slimy mucus may be present in the vomit, and streaks of blood and bile may be found. The urine is scanty and high-coloured, and deposits lithates.

Acute catarrh runs a fairly rapid course, and frequently becomes chronic. It is probably never a primary disease, unless some powerful irritant, either a poison or a poisonous food, is taken, or unless it arises in the course of an acute febrile disorder, such as typhoid fever, pneumonia, rheumatic fever, and scarlet fever.

Catarrh is sometimes subacute. It is characterised by the same symptoms, which, however, are not so severe as in the acute form. The epigastric pain and vomiting come on after food. Flatulence and nausea, with anorexia, are well-marked symptoms; and, during the course of the illness, the patient himself gradually reduces his food to a minimum. Dilatation of the stomach is a feature of subacute catarrh, and palpation of the stomach may give rise to painful peristalsis of the organ. The complexion is pale and sallow, and there is well-marked wasting. The bowels are constipated, and large quantities of mucus may be passed in the stools. The stomach contents show the characteristics as those of acute catarrh.

Diagnosis.—This will be considered more fully under the heading of "Chronic Catarrh." Here it may be said that the diagnosis of acute and subacute catarrh rest on the following points:—(1) The relation of great and diffuse epigastric pain and vomiting to the ingestion of food; (2) the presence of mucus in the stomach and in the stools; (3) the absence of pepsin and hydrochloric acid in the stomach contents; (4) the dilatation and condition of irritability of the organ.

Prognosis.—Both acute and subacute catarrh may be recovered from, if they are treated correctly. The duration of subacute catarrh is variable, and it may be months before the patient can resume an ordinary diet, and even then great care has to be exercised in the choice of food.

Treatment.—In both acute and subacute catarrh the main object of treatment is to give the stomach rest. It is usually advisable to commence the treatment by washing out the organ once or twice, preferably with a dilute alkaline solution (1 per 1000 of sodium hydrate). This removes the irritants from the organ, and frequently stops the vomiting. For the first twenty-four or thirty-six hours, or even longer, according to the condition of the patient, rectal feeding is to be adopted, by the administration of nutrient enemata every four hours. The enemata may consist of 2 oz. of milk with an egg beaten up in it, of beef-tea, and two teaspoonfuls of liquor pancreaticus, with 20 or 30 grs. of bicarbonate of sodium. This mixture must be injected warm, not hot, into the rectum. Peptonised gruel may be substituted for the beef-tea in the injection, and if the enemata cause irritation, the use of a little cocaine ointment is beneficial. Peptone suppositories, containing 60 per cent. of peptone, may occasionally be substituted for the enemata. Thirst may be relieved by a limited allowance of ice, or by the use of effervescing lozenges. If the retching still continues, a hypodermic injection of morphine may be given; and hot belladonna fomentations to the epigastrium frequently give great relief.

Feeding by the mouth must be commenced gradually, and with great care, small quantities of sterilised milk being tried every few hours at the commencement; the amount of milk being very gradually increased when it is found that it causes irritation or vomiting. When the more acute symptoms have subsided, medicinal treatment is of much value, and the best remedies are dilute hydrochloric or nitro-hydrochloric acid, in 10- to 15-minim doses, combined with 3 minims of hydrocyanic acid, or 10 minims of liquor morphinæ hydrochloratis. The later treatment is one of careful diet and of general tonics.

CHRONIC CATARRHAL GASTRITIS.

Chronic gastric irritation is frequently diagnosed as chronic catarrh; an important mistake, since gastric irritation is highly amenable to treatment, and chronic catarrh very refractory, being an inflammation of the mucous membrane associated with organic changes. Gastric irritation, however, frequently leads to chronic catarrh of the organ, the early stages of the latter being thus associated with hyperacidity. These are the cases which have been called "acid" catarrh. Chronic catarrh, on the other hand, frequently follows acute or subacute catarrh, developed in the course of a febrile illness. It is a serious affection, characterised clinically by a chronic afebrile course, with subacute exacerbations; by epigastric pain and diffuse tenderness; by the vomiting of mucus and of a liquid greatly deficient in hydrochloric acid.

Symptoms.—When insidious in origin, its early symptoms are those characteristic of gastric irritation; when established, the symptoms are mainly referable directly to the stomach and the stomach region, and are dependent on the ingestion of food, and on the delay of undigested food in the organ.

The epigastric pain begins directly after the ingestion of food, and lasts for an hour or two hours, or more. It is sometimes severe, and is only relieved by vomiting. So severe is the pain in some instances, that the patient excites vomiting to get rid of the stomach contents, and may half starve himself in fear of its onset. In milder cases, the onset of epigastric pain may be delayed some time after the ingestion of food. The pain is diffuse, burning in character, and may go through to the back. Epigastric tenderness is usually present in the course of all cases of chronic catarrh; it is diffuse and not excessive, and usually there are areas more tender than others. These tender areas have been considered to represent erosions of the mucous membrane. Epigastric tenderness disappears very soon under proper treatment, much sooner than the similar tenderness in ulcer of the stomach. When first seen, both epigastric pain and tenderness may be absent, owing to the patient having been compelled to take a diminished diet.

Nausea is frequent, even when vomiting is absent, and may come on during a meal, and so prevent the patient taking any more food. Vomiting is never absent at one or other time in the course of chronic catarrh, and in the history there are periods in which vomiting is severe; these are the periods of subacute attacks. Vomiting is usually in relation to food, but may occur in the morning. The vomited matters generally contain an excess of unpigmented mucus, and a deficient amount of hydrochloric acid. The mucus may be very abundant; it may be in strings, or flocculent and sticky. In the first class of cases it is frequently passed in the motions, as in subacute catarrh. In long-continued catarrh, there is a history of the vomiting of mucus, but at the time of seeing the patient the mucus may be absent from the vomit. Microscopically, the vomit shows strings of mucus, and a few leucocytes and goblet cells, more or less degenerated. Bacteria may be present, and a few red corpuscles may be seen. The mucus must be distinguished from the swallowed mucus coming from the bronchial tubes and lungs. This is pigmented and contains a large number of pus cells. The vomit may be slightly acid, neutral, or faintly alkaline. When there is bacterial fermentation, the vomit is highly acid, due to the presence of organic acids. There is also great deficiency of free hydrochloric acid. Pepsin is present in the mild cases, even when the hydrochloric acid is greatly diminished. According to Boas, pepsinogen may be present instead of pepsin. The vomited food is thus very imperfectly digested.

In gastric catarrh, profuse hæmatemesis does not occur. Blood may, however, occur in streaks in the vomit, or as much as 2 or 3 oz. may be brought up. Hæmatemesis, however, does not tend to recur, and is usually a sign of an erosion of the mucous membrane being present.

Flatulence is a frequent symptom in chronic catarrh, but not so marked as in gastric insufficiency and in nervous dyspepsia, unless there is bacterial fermentation of the food in the dilated stomach. Dilatation is frequently present, and presents the signs and symptoms discussed on p. 679.

In chronic catarrh the face is frequently pale and sallow; it has an

earthy complexion, and tends to become somewhat anxious-looking in cases of long standing. The appetite is usually diminished except in the early stages, and later there may be complete anorexia. Thirst may be present, especially when the stomach is dilated; the tongue is coated with a thick whitish yellow fur; the breath is often offensive. In some cases the tongue is broad and flabby. In many instances, especially in young adults, there is an enlargement and reddening of the fungiform papillæ. The bowels are usually constipated, and mucus may be present in the stools; diarrhœa is only occasionally observed. The urine, in aggravated catarrh, is passed in small amount, is not infrequently neutral or alkaline, and contains an excess of phosphates. There may be a continued diminution of the secretion of chlorides, as in other stomach conditions.

In most cases of chronic catarrh there is wasting, which may be continuous if the disease is neglected. With suitable treatment, however, the patient soon begins to regain weight. The loss of weight is increased by repeated vomiting, and especially when there is associated catarrh of the small intestine, or when catarrh is associated with a serious disease, such as pulmonary tuberculosis and chronic Bright's disease. Reflex nervous symptoms are also frequently present.

Diagnosis.—The diagnosis from chronic gastric irritation has already been discussed (p. 663). It now remains only to mention shortly its distinction from other diseases of the stomach, in which there is epigastric pain and vomiting. In ulcer, for example, there is pain directly after the ingestion of food, with vomiting, as in catarrh; but the difference lies in the fact that in ulcer the pain as well as the tenderness is usually localised, whereas in catarrh it is more diffuse, and the areas of tenderness are not so localised. Vomiting is frequent in both; but the characters of the vomited matters in ulcer show those of ordinary digesting food in the organ, or, it may be, hyperacidity, due to excess of hydrochloric acid; whereas in gastric catarrh there is an excess of mucus and a diminution in the amount of hydrochloric acid. Hæmatemesis may be profuse in ulcer; in chronic catarrh it is not common, and when present only slight in extent. It must be remembered, however, that catarrh may be associated with chronic Bright's disease, with mitral stenosis or with cirrhosis of the liver, in all of which diseases profuse hæmatemesis may occur independent of catarrh.

In cancer, epigastric pain is more irregular than in either ulcer or catarrh; it is frequently lancinating in character, and may be associated with the presence of a tumour and a greatly dilated stomach. The other symptoms of cancer are also present.

Many cases of gastric irritation, when first seen, cannot be diagnosed except by means of a test meal. By these means the question of the diminution of hydrochloric acid and of the degree of the digestive power of the stomach can be tested. Not infrequently, too, it is found in catarrh that the stomach washings contain mucus whereas no mucus was present in the vomit.

Prognosis.—If the case comes under treatment in a subacute attack, and the history of previous illness has not been a long one, a favourable prognosis may be given, if the patient be a young adult; for in these cases, by proper treatment, the catarrh diminishes and may completely heal, leaving but little or no damage in the gastric mucous membrane.

If, however, as not infrequently happens, the patient continues to

commit dietetic indiscretions, the symptoms recur, and the disease becomes aggravated, inflicting permanent injury on the stomach, even if some amelioration of the patient's condition may be obtained. In middle-aged and old people, chronic gastric catarrh is a serious affection, being much less amenable to treatment, and frequently ending in permanent damage to the digestion. When associated with tuberculosis or chronic Bright's disease, a permanent cure is not to be expected, though the disease may be partly held in check by appropriate treatment. Gastric catarrh may end in atrophy of the mucous membrane.

Treatment.—In the treatment of chronic catarrh the same general regulations as regards mode of life and general hygienic treatment are necessary as in chronic gastric irritation (p. 666 *et seq.*). Rest is essential, a rest both bodily and mental, and rest of the stomach by means of diminution of food and the administration of sedatives. It is frequently advisable to commence treatment by washing out the stomach, not only because it gives relief to the patient, but also because an examination of the stomach washings is an aid to the diagnosis of the condition of the stomach. In washing out the stomach it is best to use an alkaline solution, such as a solution of bicarbonate of sodium (3 to 6 drms. to the pint).

As regards medicinal treatment, acids are here of great value,— dilute nitro-hydrochloric and dilute hydrochloric acid, in doses of 10 to 15 mimims after food. They are usefully combined, in some cases, with dilute hydrocyanic acid or liquor morphinæ hydrochloratis, if there is much pain in the epigastrium. In other cases they have to be combined with pepsin as an aid to the digestive process. Constipation may be relieved in the manner previously indicated.

The diet in the treatment of chronic catarrh is of the greatest importance. Such patients cannot take much food, inasmuch as the stomach is incapable of coping with it. In the initial treatment a liquid diet is to be adopted. In the severer cases, peptonised milk solely; in the less severe cases, sterilised milk or skimmed milk may be used, diluted, if necessary, with water that has been boiled. It is advisable to add some salt to the milk, which must be administered regularly every two hours of the day and night. A patient on this diet must rest, and it may be some time before a change of diet is permissible. The first change that takes place being the addition to the milk, once or twice a day, of some one or other of the commercial partly digested foods, such as Benger's. If this agrees, crumb of white bread may be gradually substituted for it, and toast may be eaten. The first addition of the solid food is to be pounded boiled fish or minced chicken; and the white of an egg may now be given with milk. Change to a more solid diet than this must be very gradual, every additional article of diet being at once removed if it causes distress. During this period, both local and general massage are of great service; but, as a rule, it may be said that massage of the stomach region ought not to be performed in chronic gastric catarrh, inasmuch as it irritates the organ. In some cases the administration of small doses of alkalies, such as 10 grs. of bicarbonate of sodium before food, is beneficial when the patient is recovering, tending to stimulate the secretion of the gastric juice. Bitters, as a rule, aggravate the condition, and there may be well-marked intolerance of them. Tonics may have to be given, but only in small doses.

ACUTE TOXIC GASTRITIS.

Toxic gastritis is the inflammation of the stomach produced by the swallowing of corrosive or irritant poisons. Infective gastritis (gastritis mycotica) results from the invasion of the stomach by pathogenic bacteria.

Etiology.—The poisons which produce toxic gastritis are—(1) sulphuric, hydrochloric, and nitric acids; (2) caustic alkalis, such as potash; (3) oxalic acid, carbolic acid, and nitrobenzol; (4) arsenious acid, corrosive sublimate, potassium cyanide, chlorate of potassium, phosphorus. Phosphorus has not usually a direct corrosive action on the mucous membrane, but it produces a well-marked fatty degeneration of the glands as well as of the muscular coat. The other poisons act as corrosives or great irritants, producing here and there in the stomach destruction of the mucous membrane and intense inflammation, which is shown by swelling and reddening, and by the extravasation of blood. The results of this action, if the patient lives, are—(1) That in the parts most affected by the poison ulcers are formed, sometimes at the cardiac orifice, sometimes in the mid-region of the stomach, and sometimes near the pylorus. These ulcers run the course of the chronic ulcer of the stomach. (2) In the parts less affected by the poison, chronic inflammation is set up, as shown by the excessive secretion of the mucus. There is, however, subsequently fibrosis of the mucous membrane, with the degeneration of the glands. Cysts may be found, as well as the condition called *état mamelloné.*

Symptoms.—The symptoms are those of acute gastritis, the pain being great, the vomiting frequent, and the epigastric tenderness severe. The appetite is lost, and intense thirst is frequently present. Collapse is common, with a cold, clammy skin and a rapid pulse. Giddiness is frequent after the first effects of the poison have passed off. Albuminuria and hæmaturia are not uncommon. The vomited matters consist of the ordinary contents of the stomach, with mucus, stained with more or less altered blood, and by the poison itself. It may thus be either strongly acid or strongly alkaline or neutral. Blood in the vomit may be due to poisoning by mineral acids, or caustic alkalies, arsenic, corrosive sublimate, and phosphorus. With caustic alkalies the blood is brown or black, and is diffused through a very tenacious mucus. When the patient does not die from the immediate effects of the poison, the subsequent history of the case is either one of subacute or chronic gastric catarrh; or of permanent gastric insufficiency, due to destruction of the mucous membrane; or, it may be, of chronic ulcer.

Diagnosis.—For the special diagnosis, works on toxicology must be consulted. All that it is necessary to say here is, that in the diagnosis of acute gastritis due to poison, the suddenness of the onset of the symptoms without previous illness, their severity, and the character of the vomited matters, as a rule, render the diagnosis simple; as well as the fact that there is a clear history of all the symptoms appearing suddenly after the patient has drunk some liquid or eaten some food.

Poisoning by foods frequently gives rise to very severe gastric symptoms, like those of toxic gastritis. In this case the history is of symptoms coming on directly after partaking of a particular meal, and also of the fact that other members of the same family are affected by the same disease. The symptoms are gastro-intestinal, and consist in vomiting and diarrhœa, pains, and great prostration; subsequently, fever may be developed. Death

may occur in coma. Food poisoning arises from pork in its various forms, but sometimes from other kinds of meats, sometimes from tinned salmon and sardines.

INFECTIVE GASTRITIS.

Etiology.—The stomach is sometimes the seat of specific lesions of certain infective disorders. In diphtheria, in rare instances, the mucous membrane may be covered by a false membrane. In smallpox, an eruption may be present; and tuberculosis, typhoid, and syphilitic ulcers of the mucous membrane are amongst the rarities of post-mortem examinations. The term phlegmonous gastritis is applied to cases where either a single abscess is formed in the stomach wall, or where there is diffuse inflammation of the submucosa, due to bacterial invasion, ending in the formation of multiple foci of suppuration. A single large abscess of the stomach is not common, and is diagnosed by the discharge of pus in the vomit. Multiple suppuration may lead to numerous ulcers of the mucous membrane, and is usually associated with peritonitis. Other cases of bacterial infection of the stomach have been described. Fränkel described a case of diffuse inflammation of the submucosa, associated with effusion of blood and the formation of bladders of gas. This occurred in a man who had sustained a compound fracture of the right index-finger. The symptoms were those of acute gastritis with jaundice, death occurring two and a half days after the onset of the symptoms. Klebs described two cases, under the heading of "gastritis bacillaris"; and in anthrax the stomach may be infected by micro-organisms.

Most of the cases of infective gastritis are secondary to a general infection of the body. Deininger has published a case which was apparently primary—a case of diffuse suppuration occurring in a drunkard, with well-marked cirrhosis of the liver. The majority of cases of infective gastritis are chiefly of pathological interest. Recovery may take place, and scars be left in the position of the abscesses (Diettrich).

ATROPHY AND DEGENERATIONS.

The degeneration of the glands of the stomach occurs, as has been seen, as the result of inflammation. It may be non-inflammatory. Degenerations may be divided into three classes —(1) primary atrophy; (2) fatty degeneration of the glands, occurring in cancer of the stomach or of other parts of the body, and in some cases of long-standing ulcer; (3) albuminoid degeneration.

Primary atrophy of the stomach is not very common, and occurs usually in persons beyond middle age, from 50 to 75 years of age. Cases, however, have been described by Rosenheim, Schirren, and others, occurring between the ages of 19 and 36. It is possible that in some of these cases the origin of the atrophy was inflammatory.

In atrophy of the stomach, the walls are greatly thinned, so as to be almost semi-transparent. The arrangement of the mucous membrane in rugæ is lost; the organ is dilated, and there is no post-mortem digestion of the mucous membrane, showing that the secretory glands are deficient in activity. Microscopically, the glands are atrophied in many parts, being absent in others and their place occupied by granules. In pernicious anæmia, atrophy of the stomach may occur. (2) Fatty degeneration occurs

in cases of cancer of the pylorus, and of cancer elsewhere. It is part of the effect of the cancerous growth on the body, and is similar to the fatty degeneration of the heart muscle, of the liver, and of the kidney cortex, which constantly occurs in such conditions. In long-standing ulcer of the stomach, a similar degeneration may occur. (3) Albuminoid degeneration occurs in long-standing cases of pulmonary tuberculosis, in syphilis, and in prolonged suppuration. In the mucous membrane the vessels are affected, as well as the muscle fibres between the glands and the connective tissue.

CIRRHOSIS.

Cirrhosis ventriculi (plastic linitis, Brinton) has been described as a chronic inflammation of the walls of the stomach, associated with hypertrophy of the muscular coat, usually involving the whole of the organ and producing contraction. I am myself not at all certain that such a disease really exists. The specimens which I have myself seen, illustrating this condition, have all proved, on microscopical examination, to be cases of diffuse cancer of the stomach (see " Cancer," p. 697).

Cirrhosis of the mucous membrane of the organ may occur as the result of catarrh, but in the disease called cirrhosis ventriculi the whole wall of the stomach is affected by fibroid change, and the capacity of the organ greatly reduced, so that it holds as little as four ounces in some cases. In post-mortem examinations one does meet with cases of malignant disease in the upper part of the abdomen, in which the stomach becomes fibroid as well as cancerous from without; and, in still rarer cases, this fibrosis of the stomach is the sequel of chronic peritonitis. But as to the existence of a primary disease such as cirrhosis ventriculi, the evidence is scanty or wanting.

HÆMORRHAGE.

Etiology.—In hæmatemesis and melæna the blood may come from the stomach, and in profuse hæmatemesis there is usually melæna. The blood which is vomited may come from various sources. It may be swallowed, or it may come from the stomach itself. (1) It may be swallowed in fracture of the base of the skull, in epistaxis, and in bleeding from the lungs or œsophagus; (2) it may come from the stomach itself, and may be due to some lesion in the stomach, some tumour or growth attached to the organ, or to some general disease of the body. In these cases bleeding may be either capillary, or due to the opening of the large vessel, vein or artery.

Bleeding may occur in venous or mechanical congestion, which affects chiefly the pyloric region of the organ, and is primarily due to dilatation of the right side of the heart, such as occurs chiefly in mitral disease of long standing, especially mitral stenosis. Venous congestion also occurs in the obstruction of the portal circulation, whether acute, as in portal thrombosis, or chronic, as in cirrhosis of the liver. In gastritis there is, as a rule, slight hæmatemesis, whether it be due to the direct action of a poison, or to catarrh.

Ulcer of the stomach is the commonest cause of hæmatemesis, and is frequently due to the opening of a large vessel. Cancer also leads to hæmatemesis. The hæmatemesis of excessive vomiting is, as a rule, very

slight. In abdominal aneurysm there may be a rupture through the stomach wall, causing death by hæmatemesis. A malignant growth in a neighbouring part may invade the stomach, ulcerating and leading to the same result.

The general diseases which lead to hæmatemesis are as follows:—Acute febrile diseases, such as tropical malarial fevers, typhus fever, and the hæmorrhagic forms of variola, scarlet fever, measles, and diphtheria; the various forms of septic fever and pyæmia; and the profound anæmias, pernicious anæmia, leucocythæmia, and scurvy. Hæmatemesis may also occur in high arterial pressure, coming on in the course of granular contracted kidney. Hæmatemesis occurring as a feature of vicarious menstruation is a doubtful point.

The bleeding in hæmatemesis may be slow or rapid; the vomiting of the blood is sudden; and in the majority of cases the bleeding is not recognised till the blood is seen in the vomit. In profuse bleeding the blood is red, and consists of the ordinary elements of blood. In other cases it is clotted and may be dark; and when it remains for a long time in the organ, it is of a tarry colour, and presents the appearance of blackish granules in the deposit, commonly referred to as "coffee grounds."

Symptoms.—The symptoms produced in bleeding from the stomach depend on the amount of blood lost; but are frequently overshadowed by the serious nature of the primary disease present, such as acute febrile disease, profound anæmias, or cancer of the organ. Profuse hæmatemesis occurring, however, in cirrhosis of the liver, or in chronic ulcer of the stomach, leads to definite symptoms. In ulcer it is usually initiated by the partaking of an indigestible meal or by some sudden exertion; the patient feels suddenly faint, with a sense of warmth, sinking or actual pain in the epigastrium; the skin becomes cold, and may be covered with a cold sweat; the pulse is increased in frequency, small and compressible. Vomiting may occur at any time. After the vomiting the patient feels relieved; in some cases he will be found lying collapsed upon the bed, with a pale, drawn face, and a very small compressible pulse. Such symptoms may indicate a continuance of the bleeding. Blood may be vomited once, twice, or three times in the same attack. After the initial stage is passed, reaction sets in; the first sign being shown, perhaps, in a faint flush of the cheeks, but more commonly in the recovery of the pulse, which becomes full and bounding, although still more frequent than normal. The return of the pulse to its normal frequency may take some days; and in patients who are much debilitated by chronic illness, the symptoms of reaction are slight or absent.

In hæmatemesis an examination of the stomach region may reveal a diffuse tenderness and no other physical signs; or there may be, as in cases of ulcer, a localised area of great tenderness, with diffuse and slighter tenderness around.

In melæna the blood may come from the stomach and duodenum, from the small intestine, from a new growth, or from some simple and infective ulceration of the intestine. In bleeding from the small intestine or stomach the stools are of a uniformly dark chocolate colour, which differs somewhat from the coal-black colour imparted to them by iron, or the metallic black tint given by bismuth.

Diagnosis.—The points to decide in cases of hæmatemesis are—(1) whether the stomach is the seat of the hæmorrhage; (2) if the stomach is

the seat of hæmorrhage, the character of the lesion present,—whether mechanical congestion, catarrh, ulcer, or cancer.

In some cases where the blood has been swallowed there is no difficulty in the diagnosis; this is specially so in cases of epistaxis. In the case of a rupture of a large artery into the upper alimentary tract, death usually ensues. It may be, however, difficult in some cases to decide whether an actual attack of hæmatemesis is due to swallowed blood from the lungs, or to a lesion of the stomach itself, although the difficulty is usually greater in deciding on these points when cross-examining a patient on his previous history. In pulmonary tuberculosis, hæmorrhage occurs in various stages of the disease—first, in the early stage; second, in the progressive stage; third, in the rupture of an aneurysm in a cavity, an event which is usually fatal. A decision between hæmoptysis and hæmatemesis is to be made by an examination of the mode in which blood is brought up, by the symptoms and physical signs present, and by the examination of blood and other matters which are ejected. In both hæmoptysis and hæmatemesis the bleeding may be at first profuse. Hæmoptysis frequently induces vomiting; but during the rest of the day, or the next few days, bleeding from the lungs continues, and the patient brings up small quantities of blood mixed with sputum, which will contain tubercle bacilli; and this, when it occurs, is characteristic of hæmoptysis. It does sometimes happen, however, that this continued spitting up of blood does not occur, and then the diagnosis rests on the physical examination; for, in bleeding from the stomach due to ulcer, there is a localised tenderness, with a previous history of pain after food and vomiting; whereas in hæmoptysis, besides the history of cough, expectoration, night sweats, and wasting, there are the physical signs at one or other apex of the lung, indicating tuberculous infiltration.

In cases of portal obstruction, the existence of ascites, of pain and tenderness in the liver region, of slight enlargement of the liver, and the proof of the alcoholic habits of the patient, are themselves diagnostic. If the bleeding is due to a general disease, the signs of the disease are so prominent as to be easily detectable such, for example, as the hæmatemesis which occurs in pernicious anæmia and in leucocythæmia.

As regards the stomach itself, the diagnosis lies between ulcer and mechanical congestion and cancer, and should be made from the general and local symptoms of these diseases. Cases of difficulty, however, arise as to the cause of the hæmatemesis when chronic renal disease or mitral stenosis are present. In both these conditions a tender stomach may be present, leading to the suspicion of ulcer of the organ, when the subsequent course of the case shows that no ulcer is present.

Prognosis.—In profuse hæmatemesis which is due to ulcer, the immediate prognosis is, as a rule, good; but the general condition of the patient and the special condition of the stomach must be taken into account, as well as the amount of blood lost. In cases of old ulcer, for example, where the patient is emaciated and worn out with pain, the occurrence of hæmatemesis frequently leads to death. In recent cases of ulcer, recovery is the rule. In cases of portal obstruction, of mitral stenosis, and of chronic renal disease, the hæmatemesis is not only, as a rule, not serious, but is actually beneficial to the patient in relieving, in the one case, the venous congestion, and in the other the high arterial tension.

Treatment. — The treatment of cases of hæmatemesis may be

summed up in rest to the body, and rest to the stomach, and abstention from all active treatment. The patient is to be kept in bed, and to remain in a recumbent position in a cool room, and is not to be excited by the visits of friends. All feeding by the mouth is to be stopped, rectal feeding being adopted, and ice being allowed to relieve the thirst. A tendency to syncope may be treated by cold applications to the temples, by inhalation of the vapour of ammonia, or by a rectal injection of brandy. Ether may also be injected subcutaneously; otherwise more vigorous treatment is not to be adopted. No stimulants are to be given by the mouth. For the prevention of a recurrence of the hæmorrhage, the stopping of all food by the mouth is usually sufficient; but astringents may also be given, namely, tannin or gallic acid in doses of 2 to 5 grs., or acetate of lead in 1 gr. doses in pill. These must be given every one, two, or three hours. If restlessness and excitement supervene after the hæmorrhage, these must be treated, either by a hypodermic injection of 2 minims of liquor morphinæ, or by a rectal injection of 15 grs. of chloral hydrate and 30 grs. of potassium bromide.

Excessive vomiting and retching may also be treated by the hypodermic injection of morphine. In the after-treatment of hæmatemesis, besides the special treatment, which is necessary for the conditions which produce it, iron is to be given in small doses by the mouth.

GASTRIC ULCER.

Ulcer of the stomach is a local disease of the organ, commencing in the mucous membrane and tending to spread through the coats, and to perforate. It exists in two forms, the acute and the chronic, both of which may lead to hæmorrhage and perforation of the organ. The chronic tends to heal, and the scar may produce a deformity; the acute may also heal, and rarely leads to deformity. Erosions of the mucous membrane are to be distinguished from ulcer; they are superficial, and on healing leave a smooth scar. Gastric ulcer is closely allied, both pathologically and clinically, to ulcer of the duodenum, which may also be acute and chronic.

Etiology.—Gastric ulcer occurs most frequently between the ages of 15 and 30 years; under 15 it is rare, and after 50 years the incidence of the disease falls. Out of 171 cases collected from the records of University College Hospital, the age incidence was as follows:—

Between	0 and 20 years	.	.	.	.	15 cases.
,,	20 ,, 30 ,,	.	.	.	.	75 ,,
,,	30 ,, 40 ,,	.	.	.	.	38 ,,
,,	40 ,, 50 ,,	.	.	.	.	25 ,,
,,	50 ,, 60 ,,	.	.	.	.	14 ,,
Over	60	,,	.	.	.	.	4 ,,

Gastric ulcer is from three to five times as frequent in women as in men. Of the 171 cases previously referred to, 144 occurred in women and twenty-seven in men, a proportion of 5·3 to 1. It is commonest in young women under the age of 30; in men, however, the tendency to ulcer increases towards middle age.

Age Incidence in Sex of Ulcer.

	0 to 20 years.	20 to 30 years.	30 to 40 years.	40 to 50 years.	50 to 60 years.	Over 60 years.	Total.
Women .	14 cases	70 cases	32 cases	15 cases	10 cases	3 cases	144
Men .	1 ,,	5 ,,	6 ,,	10 ,,	4 ,,	1 ,,	27

Occupation appears to have but little influence upon the production of gastric ulcer. Its frequent occurrence in domestic servants and in work-girls perhaps points to the coarse food eaten; more especially, perhaps, to the large excess of vegetable food partaken of by these people, containing an excess of cellulose.

Gastric ulcer may exist by itself, and be the sole organic disease present during life or found at death. It may, however, be associated with other diseases, which may of themselves be fatal or progressing at the time of death. Ague and syphilis are supposed to have some relation to gastric ulcer, but the connection must be a very remote one. They are both diseases, however, which produce anæmia, and thus may conduce to ulceration. Tuberculosis may be associated with gastric ulcer, and in some cases of pulmonary tuberculosis it is found; very rarely the ulcer is tuberculous. Tuberculosis, however, is not present in cases of gastric ulcer in greater proportion than its average incidence in individuals generally. In portal obstruction and in cardiac disease, leading to embarrassment of the circulation of the right side of the heart, ulcer of the stomach is sometimes found. Here it may perhaps be considered that the mechanical congestion of the stomach predisposes to ulceration. Chronic renal disease may also be found. With the chlorosis of young women, ulcer appears to have a definite connection. The symptoms of chlorosis may be present at the time when the symptoms of ulcer are observed, or there may be a history of some previous attack. It may be that in chlorosis it is the anæmia, as well as the altered relation between the arteries and the tissues, which predisposes to ulceration. The connection of amenorrhœa and the puerperal state with ulcer, is probably only fanciful. A more definite connection is perhaps to be made out between gastric ulcer and the pyæmic and septicæmic conditions, and the same may be said with regard to duodenal ulcer. As a rule, in these conditions the ulcer is acute and is frequently multiple, two, three, or more being present; and in all probability the direct cause of the ulceration is septic embolism. It is also probable that the occurrence of gastric ulcer and of duodenal ulcer in extensive burns of the skin is associated with embolism.

Morbid anatomy.—Acute ulcer.—The acute ulcer is usually small, varying from half an inch to one and a half inches in diameter, and has the appearance of being punched out of the walls of the stomach or duodenum. It frequently perforates; the rupture of the peritoneum being round or ragged. The edges of the ulcer are not greatly thickened, but are congested, and the base of the ulcer may show patches of necrosed tissue. Two ulcers may be found close together, varying in size, or an acute ulcer may be situated near a large chronic one. The ulcers are situated chiefly in the pyloric region and, in the duodenum, usually in the first horizontal portion.

Chronic ulcer.—The chronic ulcer is funnel-shaped, the wider end of the funnel being at the mucous membrane, the smaller being situated near the peritoneal coat of the organ. The edges are often greatly thickened. They may be one inch in thickness. The thickening is due chiefly to an increase of the fibrous tissue in the submucous coat; but on closer examination the mucous membrane, as well as the muscular and peritoneal coats, are found thickened. Sometimes the muscle appears hypertrophied towards the edge of an ulcer, but this is due chiefly to the solution of continuity of the muscle, which retracts. The base of the ulcer is irregular, owing to the ledges formed by the coats of the organ. It may be of a uniform brown colour, due to the action of the gastric juice on the blood in the superficial capillaries. It may be formed in the centre by the peritoneum alone, or the peritoneum may have disappeared, and the base be formed by the surface of the liver, pancreas, or spleen. The muscular base of the ulcer is often extensive. It appears to resist the chronic ulcerative process to a greater extent than the mucous membrane. Not infrequently part of the base of the ulcer may show a smooth scar where healing has taken place, the remaining part showing active ulceration. Adhesions are formed between the ulcer and the solid organ, opposite to it, most frequently to the pancreas, less frequently to the liver, and only occasionally to the spleen or mesentery. Adhesion of an ulcer to the anterior of the abdominal wall is rare, perforation being common when the ulcer is situated in the anterior wall of the stomach. The shape of the ulcer is round or oval; it may be horse-shoe shaped, passing from the posterior surface of the organ across the lesser curvature to the anterior surface. In size it varies from half an inch to an inch, or even as much as six inches in diameter. The ulcer is usually situated in the pyloric region of the stomach, either on the posterior surface or the lesser curvature. The following table, given by Brinton, of 216 cases examined post-mortem, shows the relative frequency of site:—

On the posterior surface . . .	86 cases,	equal to	40	per cent.
On the lesser curvature . . .	56 ,,	,,	26	,,
At the pylorus	32 ,,	,,	15	,,
On the anterior and posterior surfaces	13 ,,	,,	6	,,
On the anterior surface only . .	10 ,,	,,	4·6	,,
On the greater curvature . . .	5 ,,	,,	2·3	,,
On the cardiac pouch . . .	4 ,,	,,	2	,,

The conclusion to be drawn is, that more than three-quarters of the ulcers are to be found in the pyloric region of the stomach.

Results of ulcer.—The ulcer may either cicatrise or perforate. Cicatrisation is frequent. According to Brinton, to 156 open ulcers, there were 147 scars found on post-mortem, a proportion of 13 to 12. The scar, if large, may by contracting distort the stomach, producing either great puckering of the mucous membrane, or contraction of the middle of the organ or of the pyloric region, resulting in an hour-glass stomach, or in some cases producing an approximation of the œsophageal and pyloric openings of the organ. Ulcers of the pylorus in healing may lead to pyloric stenosis. Perforation may either be part of the chronic ulcerative process, or it may be an acute process added to the chronic; or it may be due to the rupture of the thin peritoneal base of the ulcer by some muscular effort. It is most common in ulcers of the anterior surface, and of the greater curve; it also occurs in those situated on the posterior

surface of the organ. Perforation may lead to general peritonitis or to subphrenic abscess.

Pathology.—The pathology of ulcer of the stomach and duodenum is very obscure, and no correct explanation of its occurrence is forthcoming. To produce ulceration in any part of the body a necrosis or death of the tissue must first occur. The three common causes of death of tissue preceding ulceration are—first, mechanical and chemical causes, such as corrosive poisons, etc.; second, interference with the vitality of the tissue by means of blocking of the circulation, as in thrombosis and embolism; third, bacterial infection—the invasion of the tissue by certain bacteria leading to death; and this necrosis may be attended by no signs of active inflammation. As regards the mechanical causes of ulcer of the stomach, there is no evidence that an injury can produce a chronic ulcer. A mechanical lesion of the mucous membrane of the normal stomach readily heals, as has been proved by experiment. Poisoning, however, by corrosives, mineral acids, or alkalies may lead to chronic ulcer of the stomach; these ulcers may occur, not only at the cardiac orifice but at the pylorus. Ulceration of the stomach may also occur from pressure, as when an aneurysm is adherent to the organ; or, in rarer cases, where there are fibro-myomata in the submucous coat, which become adherent to the mucous coat, and lead to ulceration. One such case I have known. Virchow promulgated the theory that a chronic ulcer was produced by thrombosis of the end arteries of the stomach, and that the shape of the ulcer is such as would be produced if the end artery were blocked. It must be said, however, that considering the frequent occurrence of chlorosis in association with gastric ulcer, this theory of thrombosis does not seem to explain all the cases. There does not, for example, seem to be any reason why thrombosis should occur only in the stomach in cases of chlorosis. Embolism, however, is no doubt the cause of ulceration which occurs in the stomach, and duodenum in septic and pyæmic conditions. It is possible that the necrosis which precedes ulceration may in some cases be due to the invasion of bacteria. In this connection it must be remembered that the most frequent site of the ulcer is the pyloric region, the region in which the glands do not secrete hydrochloric acid. The hydrochloric acid of the gastric juice is a great inhibitor of bacterial growth; and it is not difficult to suppose that the bacteria which are present in the stomach contents may in some cases persist when there is a diminished resistance to disease; and that they enter the glands in the pyloric region, and grow in the deeper parts of the glands and in the submucous tissue. Although in animals I have observed bacterial necrosis as a cause of duodenal ulceration, yet, with regard to the human subject, this idea of the formation of gastric ulcer must be considered as simple speculation.

In a large number of cases of gastric ulcer, especially in the early stage, there is hypersecretion of hydrochloric acid, and this is no doubt due, partly to the actual presence of an ulcer, which acts as an irritant, and partly to the irritation produced by unsuitable food. Hyperacidity, due to organic acids, the product of bacterial fermentation, is of rare occurrence in gastric ulcer.

A diminished acidity occurs in cases of gastric ulcer, when associated with pulmonary tuberculosis or with chronic catarrh of the stomach, or in the later stages of chronic ulcer, where the patient has been worn out by pain and by a diminished quantity of food during a long period. The

secretion of pepsin is not much affected in the early stages of gastric ulcer, and in these cases, indeed, there is usually a sufficiency of gastric juice to digest the ordinary meals. The movements of the stomach are, as a rule, more frequently affected than the secretion, especially in cases of chlorosis and of tuberculosis; in such cases there may be well-marked atony. In other cases, however, there is muscular irritability. Absorption is not appreciably affected. Bacterial fermentation is practically unknown in the earlier stages of gastric ulcer, and when it does occur, it is observed in the cases of hour-glass contraction of the stomach, or in cases of dilatation following long-standing ulcer.

Symptoms.—The symptoms which are characteristic of gastric ulcer are localised pain in the epigastrium after food, vomiting, hæmatemesis, and melæna. In addition, there may be the symptoms of gastric irritation and of great irritability of the stomach. This combination of symptoms is present in the typical cases of the disease; but there are other cases which may be described as latent, inasmuch as the symptoms are indefinite of ulcer, and are those which have been described as characteristic of gastric irritation. It is these latter cases which give great difficulty in the diagnosis, and are sometimes only recognised by the occurrence of hæmatemesis or of perforation. In all cases of ulcer, as well as in cases of functional disease, a complete examination of the body has to be made for the discovery of associated diseased conditions, and in ulcer the chief diseases which must be looked for are chlorosis, cardiac disease, renal disease, and tuberculosis.

The general symptoms due to the presence of gastric ulcer are, as a rule, extremely few. The patient, in the early stage, is well nourished, with a moderate amount of subcutaneous fat. If, however, there has been a recent and profuse hæmatemesis there is well-marked pallor, and if there has been repeated vomiting there is usually wasting. There is no fever, and when this is present it indicates either perforation and its results or not uncommonly pulmonary tuberculosis. Many patients show an expression of pain in the face, which may be anxious-looking. In long-standing cases of ulcer, the patient tends to develop cachexia, is thin and weak, with a pale face, and anxious, tired expression. They show myotatic irritability, and the blood shows a great reduction in the number of red blood corpuscles and the amount of hæmoglobin they contain. These cases are associated with catarrh or with great dilatation of the organ.

Of the symptoms referable to the stomach, the chief are, pain, vomiting, and hæmatemesis. The primary cause of the pain is the presence of an open sore in the stomach wall, which is irritated by the presence of food in the organ. It is aggravated and brought out by the ingestion of food; by the movements of the organ, which commence as soon as food enters the organ; and by the increased acidity due to hydrochloric acid. When the stomach is emptied, either through the pylorus or by means of vomiting, the pain is relieved. It is sometimes relieved by posture, the relief so obtained being supposed to be due to the removal of the contents of the organ from the surface of the ulcer. So it is said that the pain of a pyloric ulcer may be relieved by lying on the left side; that of an ulcer of the posterior surface, by assuming the prone position; of an ulcer of the anterior surface, by assuming the supine position. Pain is increased by pressure, but in some cases pressure on the epigastrium relieves it. It is felt in two positions, in the epigastric region and in the back; in both

cases it is localised and is associated with local tenderness. It may, however, be circumscribed, being observed over an area only an inch in diameter. In recent hæmatemesis both the pain and tenderness may be more diffuse. In the back the pain is usually localised to a region to the left of the spine, from the tenth to the twelfth dorsal and first lumbar vertebræ. In some cases, however, it is spread over a larger area than this. The seat of the epigastric tenderness is usually over a small area, above and to the right of the umbilicus and the xiphisternal notch, or at the notch itself. Pressure on the epigastrium, in some cases, produces dorsal pain. The area of tenderness is the region where the patient experiences the greatest pain after eating or drinking; and the area of epigastric tenderness persists in its circumscribed form, without shifting its locality, during the whole course of the illness. In relapse of the ulcer the same area of tenderness is again discoverable, although it may have previously disappeared. The pain varies somewhat in character. It is usually of a heavy boring nature, and not sharp or shooting, except in rare cases. It is usually described by patients as going through to the back from the epigastrium. Actual pain is not usually felt when the stomach is empty, and when there is a continuous pain it is usually due either to the great delay of food in the stomach, to the distension of the organ by gas, and to a condition of nervous irritability, kept up by injudicious feeding or by the presence of chlorosis. The pain comes on immediately after a meal, and its onset is due to direct irritation of the ulcer by the solid food. It is kept up by the movements of the stomach and by the secretion of hydrochloric acid. Where the pain comes on later, its onset is due to the movements of the organ and to the gradually increasing acidity of the stomach contents. In some of these cases, however, there is a duodenal ulcer, and the pain is only experienced when food is expelled into the duodenum. Pain is directly relieved by vomiting, and when this does not occur it may last from four to six hours, causing great distress. In some cases it is paroxysmal, and may be aggravated at the menstrual periods. Sometimes pain in the chest is associated with the epigastric pain.

Vomiting is a symptom frequently present, and is sometimes absent. It is usually present if the pain is severe, and it comes on either directly after the ingestion of food or one or two hours later. Some cases of gastric ulcer are characterised in their history by attacks of continuous vomiting and retching. The vomited matters may consist only of the undigested or partly digested meal, containing hydrochloric acid and pepsin, the former sometimes in great excess. There is no mucus, and bacteria are absent. Blood may be present, but frequently the vomit is slightly yellow in parts, and on microscopical examination this is found to be due to the presence of red blood corpuscles.

Hæmatemesis often occurs, and the bleeding may be severe or slight. It may occur at intervals, perhaps of years, and cases are not rare where it has occurred in girlhood and recurred in middle age. Its onset is, as a rule, preceded by no warning. There may be a feeling of faintness occurring after a meal or some sudden exertion, or it may occur when the patient is in bed, after having partaken of an indigestible supper. Hæmatemesis is of importance, inasmuch as it may be the first notable symptom in gastric ulcer. It has been said to occur in 30 to 40 per cent. of cases of gastric ulcer, but the percentage is probably much higher than this. In the 171 cases from the records of University College Hospital,

previously referred to, it occurred in 144, a percentage of about 84. The profuseness of the hæmorrhage does not depend upon the size of the ulcer; a profuse and fatal hæmatemesis is usually due to the opening of a large artery, such as a branch of the splenic, of the pyloric, or of the coronary artery. Profuse hæmatemesis is usually associated with melæna. This occurs in about 11 per cent. of the cases. Out of the 171 cases referred to, melæna was observed in nineteen. In some cases, where the ulcer is near the pylorus, hæmatemesis may be absent, and melæna alone observed.

Flatulence is sometimes a severe symptom in gastric ulcer. It is not due to bacterial fermentation of the food, but to swallowed air, or one of the other causes previously discussed. The appetite is usually good, but the patients are afraid to eat owing to the distress caused by the food; the appetite may even be increased. In cases of long standing, however, the appetite fails. The tongue varies; it is usually clean, and not infrequently a broad, pale, flabby, tooth-indented tongue, as in anæmia, is observed. The bowels are usually constipated. The urine presents no great variation from the normal; in some cases albumoses are present. In the later stages of ulcer, where there has been a long history of pain and repeated attacks of vomiting, and thus consequent starvation, the patient wastes, and a slight attack of hæmatemesis may produce a fatal result. In other cases there may be great dilatation of the organ, due chiefly to long-continued atony of the wall, or to stenosis of the pylorus. There may be hour-glass contraction of the organ, or, in rare cases, stenosis of the cardiac orifice.

Course and duration.—It has been stated that 80 per cent. of the cases get well. Gastric ulcer is a disease highly amenable to treatment, which has as its object the relief of pain, and the giving of the stomach sufficient rest to allow of the healing of the ulcer. Even with the presence of an open ulcer in the organ, there are remissions in the disease, due chiefly to a non-irritating diet being taken. As a rule, however, patients in this stage become careless, take unsuitable food, and a relapse occurs, which is frequently shown by hæmatemesis or by perforation, or simply by the recrudescence of the epigastric pain.

Complications.—Perforation is a frequent cause of death, and is the event most to be dreaded in gastric ulcer. According to Brinton, in 234 cases of death from perforation, 160 were females, and seventy-four were males. In statistics quoted by Habershon, death from hæmorrhage took place in 185 cases, of whom 108 were males, and seventy-seven, women.

The frequency of perforation has been estimated by Brinton as 13½ per cent. of all cases; probably, however, it is somewhat higher than this. It is most frequent in young women, and is most likely situated towards the anterior surface of the organ. In ulcer situated on the posterior surface, the base of the ulcer may be formed by the pancreas, spleen, or liver; but perforation may occur and result in the formation of a subphrenic abscess. In other cases, the perforation, especially from ulcers on the anterior surface, is into the general peritoneal cavity, and general peritonitis occurs.

Nearly 80 per cent. of the ulcers on the anterior surface are said to perforate. Death may occur in a few hours from shock, without the development of general peritonitis. In other cases the symptoms may be divided into two stages; in the first of which there will be evidence of the rupture of a hollow viscus; in the second, the evidence of general peritonitis. The

rupture usually occurs after a meal or some sudden exertion; in a fit of sneezing or coughing, or during vomiting. There is acute pain, referred to the upper part of the abdomen, sometimes doubling the patient up, as well as faintness and vomiting. The pulse is rapid, and the features soon become pinched, drawn, and haggard. Later on, the abdominal pain becomes more diffuse. On physical examination, it may be found that the stomach contents (gas and liquid) are retained in the upper part of the abdomen, between the stomach, liver, and diaphragm, or they are present in the lower part of the abdominal cavity. In the first case the physical signs are those of subphrenic abscess. The abdomen is generally moderately distended, and there is but little movement of the diaphragm during respiration. There is diffuse tenderness over the stomach region, most acute at the seat of the perforated ulcer. Percussion may demonstrate gas and liquid in the flanks and iliac regions, but all the liquid may be collected in the pelvis. In the second stage, that of peritonitis, there is fever, ranging from 100° to 102°. The expression of pain is well marked on the face, the pulse is small and rapid; vomiting and hiccough may be present. Extreme rigidity and distension of the abdomen may obscure the physical signs over the lower two-thirds of the abdomen. Abdominal respiration is usually absent.

Subphrenic abscess, formed below the diaphragm, and above the liver, stomach, and spleen, may occur from perforation of a gastric or duodenal ulcer, from the perforation from cancer of the œsophagus or stomach, from rupture of a hydatid cyst, from typhlitis, injury, gallstones, splenic abscess, or perirenal abscess. Of seventy-eight cases of subphrenic abscess, collected by Nowack, 41 per cent. were due to perforating ulcer of the stomach or duodenum; 4 per cent. were due to perforation in cases of cancer of the stomach or œsophagus. In twenty-nine cases published by Maydl, and by Penrose and Dickinson, of cases of subphrenic abscess, the perforating ulcer was found on the posterior surface in ten cases, on the anterior surface in seven, and along the smaller curve in twelve. The abscess may be either on the left or right side of the body, according to the position of the perforating ulcer: the rupture of a duodenal ulcer, or ulcer in the pyloric region of the stomach, giving rise to right-sided subphrenic abscess; rupture of an ulcer in the cardiac end, to a left-sided subphrenic abscess. The boundaries of a right-sided subphrenic abscess are the vault of the diaphragm above, the liver below, the falciform ligament of the liver on the left, and on the right, the thoracic wall. In left-sided subphrenic abscess, the boundaries are the diaphragm above, the liver and anterior surface of the stomach below, the abdominal wall united by adhesions to the stomach in front, the falciform ligament on the right, and on the left it is bounded by adhesions between the cardiac end of the stomach, the spleen, and the diaphragm. Although primarily unilateral, the abscess may infect the other side. The contents of the abscess are pus and gas; sometimes they are sweet, sometimes foul-smelling. The remains of food may be found in a recent abscess. The perforation in the stomach may be patent or closed. An abscess in this situation excites inflammation in the lung above, resulting in pleurisy with effusion, empyema, pneumonia, pneumonic abscess or gangrene of the lung; and there may be no direct communication between the abscess and the lung. Of forty-five cases collected by Maydl, the pleura was normal in eleven, adherent in ten, contained a serous fluid in nine, and pus in fifteen cases.

The development of subphrenic abscess, due to gastric ulcer, is preceded by the symptoms which have been described as occurring in perforation of the stomach or duodenum. There is fever to a slight extent, with dyspnœa, but, as a rule, no cough or expectoration. The general condition indicates a severe illness. A physical examination shows the following points. In many cases the heart's apex-beat is displaced horizontally away from the diseased side. The side is but slightly bulged, and the respiratory movements are deficient. In some cases, abdominal respiration ceases, in others it is present. A thrill may be elicited over the abscess, in some cases, by a sudden jerking movement given to the abdominal wall. The liver may be displaced downwards, even to the level of the umbilicus. In left-sided abscess the spleen does not usually come below the costal margin. Over the lower part of the thorax there is a tympanitic note, the upper limit of which is sharply marked off from the resonance obtained over the lung. The liver dulness may be completely absent, a tympanitic note being obtained over it. A similar note may also be obtained over the lower part of the cardiac area; posteriorly, there may be dulness when the patient is lying down. The physical signs of percussion are frequently obscured by the presence of consolidation of the lung, or by fluid in the pleura. Auscultation gives valuable signs. Vesicular breath sounds are heard over the lung, down as far as the edge of the abscess; while over the tympanitic resonance the breath sounds are replaced by amphoric breathing; and over the area of dulness they are absent. The bell sound may be obtained.

Diagnosis.—The association of symptoms which have been described are very characteristic of gastric ulcer. The typical symptoms are not always present, or one may be present, such as pain, hæmatemesis being absent; or hæmatemesis may be present, without any very definite pain. For the diagnosis of the causes of hæmatemesis other than gastric ulcer, the paragraph on this subject must be referred to (p. 676). Pain after food is present in other diseases of the stomach besides gastric ulcer—in nervous dyspepsia, in gastric catarrh, and in cancer of the stomach.

In a young woman, the subject of chlorosis, where there is no renal disease and no cardiac disease, the presence of localised epigastric and dorsal pain, with tenderness coming on after food and relieved by vomiting, is sufficient for the diagnosis of gastric ulcer, whether hæmatemesis be present or not. On the other hand, in such patients, hæmatemesis may be the first symptom noticed, and its occurrence in association with slight dyspeptic symptoms is sufficient for the diagnosis. The significance of the local pain and tenderness is as great in middle-aged as in young women; but there is more tendency in the middle-aged to the recurrence of hæmatemesis, due to mitral disease or chronic renal disease, than in the young adult. Gastric ulcer must be diagnosed from gastric catarrh, nervous dyspepsia and gastralgia, cancer of the stomach, cholelithiasis, and duodenal ulcer.

In the majority of cases, ulcer of the stomach cannot be mistaken for gallstones, inasmuch as the pain in the latter is not situated in the stomach region, but to the right of it, and is extremely severe, extending all over the right hypochrondrium and to the front of the abdomen. The history of the patient may be distinctive, the localised pain and tenderness and history of hæmatemesis pointing to ulcer; the history of long intervals between the attacks of pain, with the occurrence of jaundice and tenderness of the liver, pointing to biliary colic. In the majority of cases, duodenal

ulcer is not diagnosed during life. It may be suspected, but it may give rise to no characteristic symptoms until it causes death by hæmorrhage or perforation.

Of 151 cases collected by Perry and Shaw, there were no records of notice-able symptoms in ninety-one cases; in sixty cases there was hæmatemesis and melæna in twenty-three; but in many cases there were only vague dyspeptic symptoms during life. There may be great pain following the ingestion of food, and localised in the right hypochrondrium. This pain will occur some time after food, and if associated with melæna is suggestive of duodenal ulcer; but, as in gastric ulcer, hæmatemesis may occur. In duodenal ulcer, diarrhœa may be a symptom; but it is extremely rare in gastric ulcer. It is impossible for the diagnosis between gastric and duodenal ulcer to be made in the majority of instances.

The diagnosis of rupture of a gastric ulcer from rupture of any other part of the intestinal tract is, in some cases, of great difficulty. Symptoms of shock, followed by those of general peritonitis, are common to rupture of any hollow viscus. In typhoid fever, the diagnosis is, as a rule, not difficult, owing to the history of the preceding acute illness. In rupture of a duodenal ulcer, no diagnosis is possible from that of gastric ulcer. The points to be looked for in the diagnosis of the latter are, the occur-rence of pain in the upper part of the abdomen, the absence of abdominal respiration, the distension of the abdomen, and the physical signs in the upper part of the abdomen, which will be described as subphrenic abscess.

It is not always easy to decide in subphrenic abscesses whether the collection of pus is above or below the diaphragm. Indications of its being below the diaphragm are the history of the illness; the replacement of the normal liver dulness by an area of tympanitic resonance; and the signs of pneumothorax over the abscess. When the subphrenic abscess is compli-cated by a large pleural effusion, or by consolidation, or abscess of the lung, the diagnosis of subphrenic disease may be impossible until the operation; the symptoms and signs of disease of the lung obscuring those of the abscess below the diaphragm.

Abscesses occurring on the right side of the abdomen may be due to typhlitis, or to perinephritis, or to gastric ulcer; on the left side, to ulcer or disease of the colon or kidney. The diagnosis in these cases rests on the previous history of the patient, to a great extent, on the presence or absence of pus in the urine, and in the cases of typhlitis, on the presence of the signs of disease in the right iliac region.

Prognosis.—As a rule, the prognosis is good. Not only do many cases recover, but their treatment is so clearly indicated, that, if adopted, healing of the ulcer occurs. Accidents may, however, happen at any time, such as perforation or hæmatemesis, and the only means of guarding against these results is by treatment. To some extent the prognosis depends on the associated disease, of which, as a rule, the two most serious are renal disease and tuberculosis. No prognosis can be made from the size, depth, or position of the ulcer, since there are no symptoms or physical signs enabling the diagnosis of these points to be made.

Unless operated upon, cases of subphrenic abscess end fatally, by pro-ducing putrid empyema or abscess of the lung, or general peritonitis. The pus may be discharged through the lung, or into the peritoneal cavity. Of 178 cases collected by Maydl, ninety-eight died without operation, six healed without operation; and of the seventy-four operated on, thirty-five died and thirty-nine recovered. It may therefore be looked upon

practically a fatal disease, unless relieved by operation. The treatment is indeed purely surgical. In untreated cases of perforated gastric ulcer, the results are usually fatal, either from shock or from general peritonitis. Recovery, however, has been recorded.

Treatment.—The two objects to be borne in mind in the treatment of ulcer of the stomach are—(1) to promote the healing of the ulcer; (2) to relieve the symptoms of the disease. These objects are gained by giving physiological rest to the stomach. Bodily rest is essential in the treatment of all cases of gastric ulcer with active symptoms. A non-irritating and digestible diet is also an essential, and in some cases the food must be withheld completely from the mouth, and given by rectum. Gaseous extension of the stomach is also to be prevented, and any general condition of the body present, such as anæmia, appropriately treated. With this physiological rest, the symptoms—pain, vomiting, hyperacidity, flatulence, constipation, hæmatemesis—which have to be treated, abate, and this end is gained, not only by a proper diet, but by medicinal treatment. Cases of ulcer of the stomach come under treatment in different stages of the disease. They may be only suspected cases—*i.e.* first, those in which no definite symptoms of ulcer have occurred; second, there may have been a recent bleeding in the stomach, or the bleeding may occur while the patient is under observation; third, there may be a history of hæmatemesis some time previously, but symptoms of ulcer are still present, as is shown in pain, tenderness, and vomiting; fourth, the case may be a long-standing one, and the patient may show signs of dilatation of the stomach and of profound anæmia, with wasting. Suspected cases of ulcer are to be treated as if the diagnosis were clear; cases in which there has been recent hæmatemesis have to be treated on the lines laid down on p. 679. Cases in which there is dilatation of the stomach are to be treated as advised on p. 624. We have here to consider the treatment of such cases as show localised pain, tenderness, and vomiting, without recent hæmatemesis. In those cases vomiting is not uncommonly a frequent symptom; the patient can hardly retain any food in the stomach. There may be cases where food causes severe pain. It is best to commence treatment by withholding all food from the mouth, and to continue rectal feeding for a period of two, three, or four weeks, ice being allowed for the relief of thirst. Rectal injections have previously been considered. If there is any difficulty in the retention of the nutrient enemata, 5 or 10 drops of tincture of opium may be added to them, or the nozzle of the syringe may be smeared with cocaine ointment. This treatment, by means of rectal injections, is extremely serviceable in affecting a cure in aggravated cases of gastric ulcer. In many cases, however, it need not be resorted to, and food may be given in a liquid form by the mouth. Milk—either the full milk or separated milk (sterilised)—is to be given in small quantities frequently during the day and night; and if the full milk causes much pain, separated milk alone is to be used. In some cases it is advisable to begin the treatment by using peptonised milk. Beef tea or beef jelly may be given occasionally for a change, and the milk may be flavoured either with coffee or tea. In changing from the liquid to the solid diet, great care is to be exercised in watching the effect of any addition of solid food to the dietary. It is usual to begin, once a day, with finely divided crumb of bread boiled in milk, and if this agrees, to proceed in a few days to pounded boiled fish, or minced chicken or chop. The addition of meat, however, to the dietary must be very carefully considered. The great

indication of the solid food not doing harm is the absence of pain in the epigastrium ; and, as a general rule, it may be stated that, as long as there is much pain in the epigastrium after food, solid food-stuffs must be withheld, and the patient must be kept at rest.

As regards medicinal treatment, acids are as a rule, inadmissible, and alkalies after meals are of great service in counteracting the hyperacidity which frequently occurs. They may with advantage be combined with sedatives for the relief of the pain and vomiting ; thus, 15 gr. of bicarbonate of sodium may be given, with 3 minims of dilute hydrocyanic acid, and 5 to 10 minims of liquor morphinæ hydrochloratis. In other cases, cocaine acts well in doses of $\frac{1}{10}$ gr. of the hydrochlorate, given in pill ; bromide of potassium is also of great service. Flatulence may be relieved by giving one of the antispasmodics previously mentioned ; and constipation is to be treated as already mentioned. All violent purgatives are to be avoided.

Under careful treatment patients suffering from gastric ulcer improve, and a great amelioration of the symptoms takes place within a fortnight or a month. Whenever, however, the patient feels better, he is apt to take too much food, and even indigestible food, and thus to have a relapse; whereas, for a long time—it may be a year or more—he should consider himself a dietetic invalid.

In perforation and subphrenic abscess the only treatment is surgical. The objects of an abdominal section are to cleanse the peritoneal cavity of the extruded gastric contents, and to close the opening of the ulcer. The decision as to the closing of the ulcer depends on its accessibility and on the adhesions round it. Further surgical treatment need not be discussed here.

CANCER.

Cancer of the stomach is frequently a primary disease of the organ, affecting usually the pylorus, but also the cardiac orifice and the mid-region of the stomach. Cancer of the œsophagus, in rare instances only, spreads through the cardia, and secondary growths in the stomach occur from extension from growths in the neighbourhood, and only in the form of multiple nodules. In this way sarcoma may affect the stomach, primary sarcoma of the organ being extremely rare.

Etiology.—The etiology of cancer of the stomach is that of cancer elsewhere, and need not be discussed in this place. Cancer of the stomach occurs at middle age. Of 600 cases collected by Brinton, three-fourths occurred between the ages of 40 and 70, and the greatest number between the ages of 50 and 60. The disease may occur, however, in young adults, and these are usually cases of colloid carcinoma. To some degree there is a predisposition in males to cancer of the stomach. In fifty-three cases collected from the records of University College Hospital, thirty-two occurred in males, and twenty-one in females. There is no definite relation between previous disease of the stomach, whether functional or organic, and the development of cancer. It may occur in the chronic dyspeptic, or in those who have had ulcer, and Rosenheim states that 5 per cent. of cases of ulcer pass into cancer. It might be more correctly stated that in 5 per cent. of cases of ulcer, cancer is subsequently developed. Retrograde tuberculosis of the lungs is not infrequently found in patients who have died of cancer.

Morbid anatomy.—The forms of cancer which are found in the

stomach are scirrhus, columnar, medullary, and colloid carcinoma. Scirrhus forms about three-fourths of the cases. Colloid cancer is present in about 9 per cent. of the cases, and is the form usually found in young adults. It is unnecessary here to describe microscopically the character of these various forms of cancer. Of great importance is the locality of the new growth, inasmuch as according to its position so is the effect on the stomach. The parts of the stomach where the new growths may be situated are, in the order of frequency, the pylorus, the lesser curvature, the cardia, and the greater curvature. There is another form of cancer which is diffuse, infiltrating the stomach generally, and this may also result from any of the local growths.

Brinton found the pylorus affected in 60 per cent. of the cases, Hahn in only 35 per cent.; the lesser curvature in 16 per cent. of the cases, the cardia in 10 per cent., while the greater curvature is but rarely affected.

The chief change that occurs in cancer is one of degeneration and ulceration, so that a growth which previously produced stenosis may ulcerate, so as to again open the passage. Adhesions are formed to the neighbouring organs, especially to the liver. The colon may be adherent to the stomach, and a fistula be formed, or in some cases there may be an abdominal fistula. Thrombosis of the inferior vena cava, or of the portal vein, may occur, as well as pressure on and obstruction of the thoracic duct. Secondary growths occur in about 48 per cent. of the cases. They are most frequent in the liver; thus, of fifty-three cases collected from the records of University College Hospital, the liver was affected in eighteen cases, or 30 per cent.; the peritoneum was affected in 17 per cent. of the cases. In some cases there is cancerous peritonitis, either general or limited to the pelvic region. The lungs may show discrete nodules. Of the other effects of the growth may be mentioned ascites, which is present in the later stages of cancer, and is due either to cancerous peritonitis or to portal obstruction. Jaundice may also be present, due to the liver being invaded. The kidney may be found cirrhotic, and the heart is usually fatty.

Pyloric stenosis is frequently the result of cancer. The growth may be either fungating, or it may be hard and infiltrating. Dilatation and hypertrophy of the stomach follows the stenosis. In some cases a diffuse infiltration, with slight pyloric obstruction, occurs, and the stomach assumes the form of an oval bag, or, as it is sometimes described, "like a leathern bottle." In these cases the whole of the stomach wall is fibroid and hypertrophied, as well as infiltrated with cancer. Obstruction may also be caused by a large fungating growth in the mid-region of the stomach, and the cardia may be obstructed, causing symptoms like those of stricture of the oesophagus. Perforation of the stomach occurs in about 4 per cent. of the cases; it may result in a subphrenic abscess, in a gastro-colic fistula, or, more rarely, in a gastro-cutaneous fistula.

Weakness or atony of the muscular coat is one of the earliest signs of cancer of the stomach. It is most marked when there is pyloric stenosis, and it is intensified by the anæmia, general weakness, and cachexia produced by disease. Secretion may not at once be effected, but as the disease progresses the hydrochloric acid diminishes. This diminution of hydrochloric acid is due partly to the infiltration of the stomach wall by the new growth, but also to the general condition of the body, and to the associated atrophy of the gastric glands. The great tendency in cancer with dilated stomach is to bacterial fermentation of the food, so that the

prolonged presence of lactic acid in the stomach contents is an important diagnostic sign of cancer.

Symptoms.—The symptoms present in cancer of the stomach are extremely varied, and depend to a great extent upon the position of the growth. In some cases in which the growth is situated in the mid-region of the stomach, the symptoms referable to that organ are extremely few, there being only the general symptoms of malnutrition and anæmia associated with cancerous disease. When the growth is situated at the pylorus and produces stenosis, the symptoms referable to the stomach are well marked, inasmuch as great dilatation of the organ ensues, with bacterial fermentation and repeated vomiting. When the growth is situated at the cardia the stomach symptoms may be extremely few in number, and the signs of the disease closely resemble those of stricture of the œsophagus.

The course of malignant disease may be divided into three stages, in the first of which the symptoms are insidious and indefinite; in the second of which there is developed a definite tumour, with increase of pain and tenderness; and in the third, preceding death, in which complications are likely to arise.

Where a tumour cannot be recognised, a correct appreciation of the case is very difficult, and, as a rule, the diagnosis can only be made in the second and third stages. The signs and symptoms due to the growth itself may be summed up as pain and tenderness, hæmorrhage, and the existence of a primary tumour and of secondary tumours. The pain is usually sharp and shooting, and may, when it infiltrates the liver, be dull and boring. It is localised, and is accompanied by local tenderness. Malignant tumours lead to two forms of hæmorrhage; one of which is slow and is due to the ulceration of the growth, and the other of which is profuse, and often fatal, and is due to the opening of a large vein or artery. The tumour itself, which can at first be felt as a resistance, increases and becomes nodular.

The general symptoms of cancer are those of wasting, anæmia, with an opaque, earthly, pallid complexion, and a sense of great weakness. Fever is not present, unless there are complications, such as the formation of an abscess following perforation, or the formation of a gangrenous patch outside the hollow viscus. Death may occur from exhaustion, starvation, from hæmorrhage, from abscesses, and from anæmia or bronchitis.

A typical case of cancer of the stomach may be described as follows:— A patient, middle-aged, commences to suffer from symptoms of indigestion of food, the chief signs of which are loss of appetite, which may be extreme, some nausea, and pain in the chest after eating. The effect of these symptoms is out of all proportion to their severity. Wasting is rapid, great pallor ensues, while there are no physical signs of organic disease in the thorax or abdomen, and no renal disease to account for the effect on the general nutrition. Vomiting, irregular in its onset, follows, the vomit containing bacteria, sarcina, and an excess of organic acids. The stomach may be found dilated, and the epigastric pain is localised over the pylorus, and is associated with tenderness. A tumour may here be discovered, nodular and movable. Hæmorrhage may occur, although cases are observed in which hæmorrhage is never present. The case is one which goes progressively downwards. Loss of appetite occurs in 85 per cent. of the cases of cancer, presenting a great contrast of ulcer. The tongue is usually broad, pale, and flabby. Pain is present in 92 per cent. of the cases; the seat is usually epigastric, and it may, like that of ulcer, spread through to

the back. It is not necessarily related to the ingestion of food, and it is not greatly relieved by vomiting. Vomiting occurs in 87 per cent. of the cases, and presents the characters of dilatation of the stomach (*q.v.*). Hæmatemesis occurs in 35 to 40 per cent. of the cases, and is thus less frequently observed than in ulcer. The blood is frequently tarry in appearance, or like coffee-grounds; although the presence of this kind of blood does not necessarily indicate cancer. The wasting in some cases is progressive; but in others—owing to the adoption of treatment for the relief of bacterial fermentation—there may even be a slight gain in weight at one period of the disease. The bowels are usually constipated, diarrhœa occurring in 35 per cent. of the cases. Melæna is not a common symptom. The urine presents the characteristics of those of dilatation of the stomach.

Two classes of cases are met with, namely, those where there is no tumour to be felt, but there is dilatation of the organ; and those where a tumour is present, with or without dilatation. These present the physical signs previously described. Peristalsis may occur, being observed mostly in cases of pyloric stenosis. In cases where there is diffuse infiltration of the stomach, the organ forms an oblong tumour across the abdomen, usually tender and hard, which cannot be inflated. When there is a tumour present, it may be discovered over the pylorus, or over the cardia, or along the lesser curve. These tumours are hard, irregular, movable, and tender. They vary in some degree according to their position, and their movability may be extremely marked, perhaps over an area with a radius of 4 or 5 inches. Such a tumour moves downwards on deep inspiration, but is not affected to any extent by expiration. Frequently gurgling is felt by pressing the gas in the stomach through the tumour. Small tumours round the cardia may be discovered only by the passage of the œsophageal bougie, but frequently they spread over the cardiac pouch, presenting themselves as a flat mass below the left hypochondrium.

The secondary growths in the liver may be so large as to obscure the stomach tumour, and the case may be diagnosed as one of primary cancer of the liver; whereas, on a post-mortem examination, it is found to be, primarily, cancer of the stomach. Jaundice occurs in about 5 per cent. of the cases; œdema of the legs in about 12 per cent.; and albuminuria is not infrequently present.

Course and duration.—Cancer of the stomach is always a fatal disease. It may kill within a few months, or cases may last even thirty-six months; the average duration being probably about eighteen months. Amelioration of the condition may be produced by careful dieting, and by counteracting bacterial fermentation of the food.

Diagnosis.—In cases of cancer which present themselves with no tumour, but with dilatation of the organ, there is frequently great difficulty in diagnosis; such dilatation may be due to catarrh or to old ulcer. The history of the case, which is prolonged in cases of ulcer and catarrh, must be taken into account, as well as the age of the patient, and the greater severity of the symptoms in cancer. When a tumour is present in the stomach region, it may be a simple tumour of the pancreas or a tumour of the gall bladder. The history of the patient in this instance separates the case from that of cancer. The presence of a tumour of the pylorus, with great dilatation of the stomach, points to a pyloric stenosis; that of a mass below the left hypochondrium, associated with stenosis, points to cancer of the cardia.

Treatment.—The treatment is only palliative, and is directed to the relief of pain by means of sedatives, especially morphine, for the relief of constipation, and for the counteracting of the bacterial fermentation of food by means of antifermentatives, and the other methods described in the paragraph on " Dilatation." The diet to be adopted must be on the lines previously laid down. The surgical procedures which have been carried out for cancer of the stomach are mainly palliative. Excision of the pyloric growth (pylorectomy) is attended by a large mortality, but in some of the cases of recovery has caused a great amelioration of the symptoms. It is only permissible if the growth be small. In the majority of cases the size of the growth can only be determined by an abdominal section. The second operation, that of gastro-enterostomy, which has been performed in pyloric cancer, is only palliative, and serves, by the relief of the pyloric stenosis, to stop the bacterial fermentation of the stomach contents. The mortality attending the operation is high, but substantial relief, resulting in the prolongation of life, has resulted in some cases.

DILATATION.

Dilatation of the stomach is one of the most important conditions to which the stomach is subject; inasmuch as, when dilatation is present, the muscular power being deficient, the food is delayed in the organ, which may, in extreme cases, not be able to empty itself at all. Not only is there muscular weakness in dilatation, but there is also a distending force which keeps up the condition, and may to some extent produce it.

Etiology.—The causes of the muscular weakness of the stomach wall are chiefly two in number. First, the stomach muscles may have more work to do than they can accomplish ; second, there may be a primary weakness of the muscular wall. The stomach may have more work to do in the repetition of large meals through a number of years, so that, especially towards middle age, the muscular power is insufficient to expel the food through the duodenum, and there is delay of food in the organ. But the chief cases of dilatation which occur under this heading are those due to the narrowing of the pyloric orifice. This is usually due to cancer, but may be due to stricture caused by a cicatrised ulcer. In organic obstruction the stomach hypertrophies, but the permanent result is one of dilatation. Some cases are simple ones of dilatation, which occur as the result of primary weakness of the muscular wall. They are of great importance, inasmuch as they are extremely common, and frequently the dilatation keeps up the functional disorder. Weakness of the muscular wall (atony, myasthenia) occurs in cases of gastric insufficiency. It is associated with anæmia, with cases in which there is disordered innervation of the stomach, as in nervous dyspepsia; and it also is the sequel of acute febrile disease, such as pneumonia, typhoid fever, rheumatic fever, scarlet fever, measles, and others. This last group constitutes a large and important class of cases.

The distending force in dilatation is mainly the accumulation of gas in the organ, especially when a large amount of this is produced by bacterial fermentation of food. Practically, dilatation of the stomach is best classified under the headings of obstructive and non-obstructive.

Obstructive dilatation.—This occurs in—(1) stenosis of the pylorus, caused by cancer or fibroid contraction, as from chronic ulcer ; (2) pressure

on the duodenum by a new growth or stricture of the duodenum, following the healing of a duodenal ulcer; (3) contraction of the pylorus by adhesions in chronic peritonitis; (4) traction of the cardiac end of the stomach by adhesions, resulting from a severe and chronic left-sided pleurisy.

Non-obstructive dilatation.—This may be—(1) a sequel of gastric irritation, in this case frequently being only temporary in character; (2) gastric insufficiency, which accompanies anæmia and follows acute febrile diseases; (3) a result of subacute chronic catarrh.

Pathology.—The process of digestion is imperfect in all cases where there is dilatation, but varies according to the cause of the condition. In gastric irritation, for example, there is usually hypersecretion of hydrochloric acid, associated with a moderate degree of dilatation. Here the chemical processes are active, but there is mechanical deficiency. In the case of gastric insufficiency there is a general diminution of the functions of the stomach. In catarrh there is a great diminution, which is more marked in cancer of the organ. Cases of ulcer resemble those of gastric irritation, in the fact that the chemical processes are active. Where there is a diminution of hydrochloric acid in the organ, the usual result of dilatation follows, namely, bacterial fermentation of the food; and, in addition to this, the pylorus frequently allows the contents of the duodenum to enter the stomach, so that bile, and often pancreatic juice, may be found in the stomach contents. Gases also pass into the stomach from the small intestine and lead to one form of flatulence.

Bacterial fermentation.—Numbers of bacteria are taken into the stomach with food, but their development is normally hindered by the presence of hydrochloric acid and gastric juice. The aseptic nature of gastric juice was demonstrated by Beaumont in the case of Alexis St. Martin, and previous to him by Spallanzani. There is no doubt that this action of the hydrochloric acid as an antiseptic is an important one, although it is not judicious to go so far as Bunge in saying that it is the chief action of the gastric juice. The hydrochloric acid of the stomach does not kill the majority of the bacteria taken in food, but hinders their development, and the spores of the bacteria pass more readily through the organ than the developed forms. The forms of bacterial fermentation which occur in the stomach are the acid fermentation and the alcoholic fermentation; both of these affecting carbohydrates. Putrefaction, in which the proteids are decomposed, is of rare occurrence in the organ.

Acid fermentation is of three kinds—lactic acid fermentation, butyric acid, and acetic acid fermentation. The lactic acid fermentation is produced by the *B. acidi lactici* (Pasteur, Lister), which is the cause of sour milk, and is found in beet juice and in sour grapes. Its form is that of short thick cells, usually united in pairs, and forming spores in milk. For its growth oxygen is necessary, and it can be cultivated on gelatin and various liquid media. It decomposes milk sugar, cane sugar, dextrine, and mannite, forming a large quantity of lactic acid, together with carbonic acid gas. Starch is first converted into sugar. Butyric acid fermentation is due to the *B. butyricus.* This bacillus occurs widely distributed, and is found in decaying vegetable infusions and old cheese, and in milk kept a long time. It consists of long slender rods, actively motile and forming threads and spores. Oxygen interferes with its growth. From starch, dextrine, and cane sugar it forms a large quantity of butyric acid with carbonic acid gas and hydrogen, and transforms lactic acid into butyric acid with the formation of the same gases. The acetic acid fermentation,

due to the *Mycoderma aceti*, does not commonly occur in the stomach; the acetic acid which is found in some cases of bacterial fermentation being probably the produce of the fermentation by yeast. *Sarcina ventriculi* (Goodsir) is an acid-producing micro-organism, but its exact rôle in bacterial fermentation in the stomach is not yet known. When found in the stomach it is always a sign of bacterial fermentation. It occurs in colourless or brownish cells, 2·5 μ in diameter, arranged into groups of eight, unifed into larger masses; they look like corded bales of cotton.

Alcoholic fermentation, due to one or other variety of yeast, usually saccharomyces ellipsoideus, occurs in the stomach, and from its action on carbohydrates produces alcohol with succinic and acetic acids and carbonic acid gas. Glucose and maltose are more readily acted on than starch, gum, and cane sugar. Alcoholic fermentation is not nearly so common as the lactic acid fermentation and butyric. Putrefaction is a rare condition in the stomach, and all that need be said about it in this place is that it leads to the production of acid bodies, as well as of foul-smelling and inflammable gases. Poisonous bodies may also be produced.

The total amount of acidity of the stomach contents, due to bacterial fermentation, may be very high; thus, in one case it was found to equal the acidity of 0·48 hydrochloric acid, the acids present being lactic, but chiefly butyric acid. In other cases acetic acid was the chief acid present. The amount of lactic acid that may be present in the stomach contents varies considerably. It may be 0·149 per cent., up to 0·63 per cent.

The gases which are eructated in cases of dilated stomach, consist chiefly of carbonic acid and hydrogen, sometimes marsh gas and sulphuretted hydrogen are present. If the gas is inflammable, as it sometimes is, this quality is due chiefly to the hydrogen and marsh gas present. Nitrogen and oxygen, which are present in the eructated gas, come partly from swallowed air, and are partly due to what is called intestinal respiration; that is, the interchange of gas between the blood and the intestinal contents.

Symptoms.—The symptoms of dilatation of the stomach are both local—that is, referred to the stomach region—and reflex. The latter symptoms are the same as those which occur in other cases of disordered digestion. The association of tetany with dilated stomach has not infrequently been observed. It is possible that the tetany and dilatation may be part of a general condition, that is, may result from some preceding infection. The stomach symptoms, as a rule, have no very direct reference to the ingestion of food, although there are many exceptions to this. The symptoms may come on four, five, or six hours after a meal, or may come on only towards the end of the day, or at intervals of two or three days. They are epigastric distress and pain, vomiting and gaseous eructations. The epigastric distress and pain precede the vomiting, the pain being diffuse all over the stomach region; the symptoms are very severe, and are accompanied by a hot burning sensation which immediately precedes the act of vomiting. This gives relief, and patients get into the habit of exciting vomiting in order to relieve their distress. The amount of fluid vomited may be as much as six pints. It possesses the characters previously described, and may contain bile; bile, however, is not constantly present unless there is duodenal obstruction beyond the end of the common bile duct. Flatulence is frequently a severe symptom, and is constantly present. It is very severe during the accumulation of the

liquid in the stomach, but, after vomiting, a large quantity of gas may accumulate and blow out the stomach. The presence of a greatly dilated stomach in the abdomen affects the circulation and respiration, and when the dilatation is very acute, both respiration and the action of the heart may be seriously embarrassed, and death may ensue (Hilton Fagge). In chronic dilatation, dyspnœa is frequently present, as well as rapidity or irregularity of the pulse, and relief is given to both these symptoms by the removal of the stomach contents. The appetite is diminished, and there may be complete anorexia. In some cases the appetite is retained for a time, and there may occasionally be hunger. Thirst is a symptom which is usually present, as well as xerostomia, and both these symptoms may give rise to great distress.

Wasting is constantly observed, and there may be emaciation. The loss is not infrequently very rapid, and the gain by applying appropriate treatment is also frequently rapid. The loss of weight, no doubt, is to be ascribed to the fact that the food not only is not properly digested, but is not absorbed. The bowels are obstinately constipated. But when bacterial fermentation spreads along the intestinal tract, the motions may be loose and offensive, and there may be great distension of the large gut. As a rule, a small quantity of urine is passed, of high specific gravity, containing an excess of phosphates and a large quantity of ethereal hydrogen sulphates.

Physical examination.—The physical signs vary according to whether the stomach is distended with liquid or gas or not, and it may be advisable to distend the organ artificially, by making the patient drink 15 to 30 gr. of citric or tartaric acid dissolved in half a tumbler of water, followed by a similar quantity of bicarbonate of sodium in half a tumbler of water. In some cases the dilated stomach retains more or less its position in the epigastrium. Sometimes, however, a heavy stomach sinks into the abdomen, a condition which is called gastroptosis. In the distended and dilated stomach there is a prominent swelling over the epigastric region, more commonly occupying the lower epigastric and the upper umbilical regions. This swelling, which is formed by the stomach tumour, is marked by an ill-defined groove, passing usually from just above the umbilicus upwards in a slanting direction towards the left hypochondrium. The lower limit of the tumour is not well marked, being very indistinct on the right and left sides. Peristaltic action is frequently observed, and may be excited by rapid rubbing of the surface of the tumour. It is very characteristic, inasmuch as the peristaltic waves pass from the direction of the left hypochondrium downwards to the right towards the umbilicus. The waves do not start exactly at the costal margin, but a short distance below it. Peristalsis in this direction is characteristic of the stomach contractions. It may be present, not only when there is stenosis of the pylorus, but in dilatation due to catarrh or to functional disorder. When the stomach is empty no vermicular action is seen, and if the distension is very great it is also absent.

By palpation the limits of the stomach tumour are better defined than by inspection, there being over the stomach tumour a greater resistance than over the rest of the abdomen. If greatly distended, the stomach tumour feels like a hard ball. Splashing is a sign which is produced by a sudden jerk of the hand placed over the distended organ. Pulsation of the upper part of the abdomen may be present. In some cases a systolic epigastric thrill may be felt. By percussion, the area of the stomach

may be sometimes mapped out. In many cases, however, one cannot rely on discovering dilatation of the organ by means of percussion. In cases of moderate dilatation, the stomach note, which is short, high-pitched, and somewhat musical, is obtained in the lower part of the left axillary region, backwards as far as the posterior axillary line, upwards as far as the fourth rib. The upper limit of the stomach note varies according to the distension of the organ; and if the cardiac extremity is permanently fixed by adhesion, the stomach note is permanent in the axillary region. By auscultation, splashing in the organ may be heard if the patient, for example, be given two or three ounces of water to drink.

The area of the stomach distended with gas is sometimes easily mapped out by means of the bell sound (auscultatory percussion). It is done by placing the end of the stethoscope over the stomach in the epigastrium and tapping one coin on another in radiating lines downwards from this position. Directly the coins are moved away from the surface of the organ the bell sound ceases. Both stethoscope and coins must be pressed firmly on to the surface of the abdomen. The presence of a dilated stomach may be also shown by the passage of a sound, the end of which may be felt at a greater curvature, or by determining the capacity of the organ, for the normal stomach does not retain more than $1\frac{1}{2}$ to $2\frac{1}{2}$ pints of liquid.

Diagnosis.—The presence of a dilated stomach is indicated by the physical signs which have just been discussed; the chief symptoms being the character of the vomiting and the composition of the vomited matters. This, however, only holds good for cases of great dilatation, and in not a few cases the symptoms may be not greatly different from ordinary cases of functional disorder without dilatation, and the condition of the organ is discovered only by a physical examination. Flatulence is a symptom which is rarely absent, and its persistence—especially in young adults—in the absence of nervous dyspepsia, is frequently indicative of dilatation of the organ. A distinction has been made by some between atony of the organ and dilatation; but the condition really is one of degree: a slight weakness of the muscular coat soon leading to dilatation if dietetic irregularities are persisted in. Diagnosis of the causation of dilatation of the stomach is in many cases very difficult. The decision rests as to whether there is pyloric stenosis or not; and if stenosis is present, whether it is due to cancer or to cicatricial contraction. The presence of a tumour in the pyloric region points to pyloric stenosis; but stenosis may be present and a tumour absent.

The diagnosis of dilatation, without pyloric stenosis, rests on the previous history of the disease, such, for example, as the evidence of catarrh, or of prolonged functional disorder of the organ. In many cases no diagnosis is possible until the patient has been under treatment for some time.

Prognosis.—Although the prognosis depends on the causation of the dilatation, yet a great improvement takes place, in many cases, whether there is pyloric stenosis or not, by appropriate treatment; and it is remarkable how soon the stomach can be made to contract by means of treatment. It recovers up to a certain point, and the later contraction to its normal size takes a long time. There are some cases, however, even of functional dilatation in which prolonged treatment seems to produce no result as regards the contraction of the organ, and it has been proposed that a portion of

the organ should be excised in order to artificially reduce its size. In one case in which this was done, the results were beneficial as regards reducing the size of the organ, but no permanent benefit was obtained. It must be remembered, too, that owing to the fact that early cases of pyloric stenosis, due to cancer, are with great difficulty diagnosed, this operation ought not to be lightly undertaken.

Treatment.—The treatment of dilatation of the stomach is to be on the lines previously indicated in gastric irritation. Where there is great delay of food in the organ—as in pyloric stenosis, and where there is pronounced bacterial fermentation—washing out of the stomach, preferably by an antiseptic solution, is essential. As a rule, washing out once a day is sufficient, either in the early morning or in the evening before going to bed. The solutions which may be used are—Of boric acid, of a strength of 4 dr. to the pint; permanganate of potash, of a light pink colour; bicarbonate of sodium, containing 3 to 6 dr. to the pint; or common salt, containing 1½ dr. to the pint.

After washing out, antifermentative remedies may be administered, the best of which are—Hyposulphite of sodium, in 10- to 15- gr. doses; carbolic acid, 5- to 15- min. of the glycerinum; creasote, 1-min. doses; salicylic acid, ½ to 2 gr., much diluted; and resorcin, 5 gr.

In cases of subacute catarrh, washing out of the stomach is not to be persisted in. It may be performed once or twice at the commencement of the treatment, but, as a rule, not oftener. Much harm may be done by persisting in washing out the organ in all cases of dilatation of the stomach, inasmuch as after a time the distension of the organ, by a large quantity of added liquid, prevents the recovery from the condition. Massage, both local and general, is of great benefit in dilatation, especially when the abdominal muscles are lax, and when there is gastroptosis. In these latter cases it is frequently of benefit to wear an abdominal belt, arranged so as to press the stomach somewhat upwards. The local application of electricity may be of use, as well as douching the abdomen, if the patient can stand it.

Besides anti-fermentative remedies, it is frequently imperative to give alkalies to relieve the acidity, and antispasmodics may be useful in relieving flatulence. The diet to be given must be regulated according to the amount of vomiting and epigastric distress present. The only method of feeding in these cases is to withhold all food from the mouth and feed the patient by rectum. This is specially useful in cases of dilatation of the organ occurring in catarrh and in ulcer; but it is also useful in other cases. If the patient can take food by the mouth without much distress, it is advisable to give little liquid, and a solid diet of digestible food; thus, patients have frequently been found to do well on minced mutton, minced chicken, or meat balls, with occasionally a little milk. Carbohydrates must be withheld when there is much bacterial fermentation.

SIDNEY MARTIN.

DISEASES OF THE INTESTINES.

ENTERITIS.

THE term enteritis, or inflammation of some part of the intestine, may be applied in its strict pathological sense to a large number of morbid conditions which present wide differences in causation and in severity. The inflammation may attack any part of the intestine, from duodenum to rectum. It may be confined to the mucous membrane, as in catarrhal enteritis, or may extend to the other coats of the bowel, including the peritoneum, as in the phlegmonous enteritis set up by severe mechanical damage to the bowel. The character of the inflammation varies. It may be catarrhal—that is, confined to the mucous surface and accompanied by a non-coagulable exudation; or it may be croupous, and may lead to the death of the mucous lining and the formation of a membrane of coagulated exudation, as in croupous or diphtheritic enteritis. In many forms it leads to ulceration, as in typhoid fever and tuberculous disease of the bowels; and this ulceration may be so extreme as to form the chief feature, and lead to an incurable destructive loss of the mucous and other tissues, as in dysentery and ulcerative colitis.

As used in its simple pathological sense, the term thus comprises all inflammatory conditions of the bowels. In its clinical use, however, the term has a much narrower application. All those conditions, such as typhoid ulceration, tuberculosis and dysentery, which depend on some specific cause more or less certainly known, receive a separate description, and the term enteritis is commonly reserved for certain clinical forms of disease of which the causation is not so definitely known. The diseases, then, which come into this group are somewhat ill defined. They are loosely strung together for clinical purposes by the fact that in all of them inflammation of some portion of the bowel seems to play a part, but it will appear later that the actual inflammation may be exceedingly slight, and that in some forms it is probably a bacterial intoxication which is mainly responsible for the symptoms.

CATARRHAL ENTERITIS.

This is an inflammation limited to the mucous membrane, and accompanied by a non-coagulable mucous, serous, or purulent discharge. It may affect any part of the intestinal canal, but more particularly affects the small bowel. Clinically it is marked by diarrhœa, usually attended with pain. In adults it is of comparatively small importance, but in young children it is attended with considerable danger to life, and the infantile form deserves a separate description.

Etiology.—It may be broadly stated that most cases of catarrhal enteritis owe their origin to some irritant, which is either taken into the stomach and bowel, or is formed therein by some morbid process. Thus, food which is improper or indigestible or excessive in amount, is the most common cause, especially in the case of infants; and under this head must be included also the toxic bacterial products which are contained in decomposing food or non-sterilised milk. The medicinal use of mercury and arsenic and some purgatives, and the excessive use of the stronger

forms of alcohol, may similarly set up an intestinal catarrh. **Many** instances seem to depend in some way upon the weather and external influences. Thus it may follow directly upon exposure to cold or wet, as does a catarrh of the respiratory mucous membrane. But it is especially common in hot weather associated with drought, and it is not unlikely that the climatic condition acts in these cases through the facility afforded for the growth of bacteria in the food or in the bowel, though nothing certain is known on this point.

Lying somewhat apart from these forms is the chronic catarrhal condition of the bowels which is apt to ensue upon the passive congestion associated with cirrhosis of the liver and chronic cardiac disease. Finally, a similar condition may arise in late stages of many severe diseases, such as chronic Bright's disease, pyæmia, septicæmia, pernicious anæmia, Addison's disease, and scurvy. In such cases the intestinal catarrh may be explained, either as a direct result of the action of some circulating poison upon the bowel, or merely as an expression of the lowered tissue resistance which accompanies such grave disorders.

Morbid anatomy.—There is every reason to believe that the changes in the bowel are such as occur in catarrh of mucous membranes elsewhere, namely, hyperæmia, swelling, and dryness of the mucous membrane, followed by an increased secretion of mucus, with shedding of epithelium and some serous or even purulent exudation, often streaked with blood. There is, however, a striking disparity between the violence of the symptoms and the anatomical condition. In the post-mortem room very little change is to be seen. There may be a visible excess of mucus, perhaps blood-tinged, clinging to the surface, with patches of hyperæmia, and perhaps punctiform hæmorrhages here and there. Sometimes there may be slight swelling of the solitary follicles, and, in cases which are of long standing, abrasions or shallow ulcers (follicular ulcers) may be found on the solitary follicles and Peyer's patches.

Symptoms.—It will be understood, from a consideration of these causes, that two classes of catarrhal enteritis may be recognised. In the first class, which may be called acute, and which arises from some irritant or error in diet or climatic condition, the cause has a sudden effect, which is of short duration. In the other or chronic class the cause is persistent, and the enteritis is often a comparatively unimportant part of a general disease.

The main features of an acute catarrhal enteritis are diarrhœa and abdominal pain. It is not to be supposed that diarrhœa is synonymous with catarrhal enteritis; but at the same time it may be remembered that diarrhœa is the most constant symptom of the condition. The bowels are frequently moved, perhaps every hour in severe cases. The stools are liquid and watery, owing to the profuse serous exudation. But they always contain some bile, and are therefore yellowish or greenish, and rarely, if ever, become colourless or milky, as in cholera. There is considerable pain in acute cases, which for the most part precedes each action of the bowels; but between the actions the small intestine often shows a violent peristalsis, attended by colicky griping pain and borborygmus, as the fluid contents are forcibly driven on from section to section. Tenesmus or rectal straining is rare, and it seems only to occur when the catarrhal process affects the lower part of the large bowel. The abdomen may be unaltered in appearance, or somewhat distended. It may become sensitive to pressure after a few days of the disease. The tongue is furred, but does

not, as a rule, become dry. The appetite is lost. There may be occasional vomiting at the commencement of the attack, especially if the stomach is similarly affected. The temperature is usually normal throughout, and it seldom exceeds 101° for a few days. In very severe cases, associated with profuse diarrhœa and great loss of fluid, there may be some degree of collapse, and in debilitated individuals this may give rise to alarm; but in the majority of cases, where the trouble arises from error of diet, or originates in some weather-condition, the patient is himself again in three or four days, and there is no need for anxiety. The matter becomes more serious and more difficult to treat when it depends on some recurring or constantly acting cause, such as a cirrhotic condition of the liver. In such chronic cases the diarrhœa is often profuse and uncontrollable, while pain is rarely severe, and is often entirely absent.

The association of a catarrh of the duodenum with a similar condition in the stomach is not uncommon. It is marked by a more persistent loss of appetite, by more tendency to vomit, and by a sensation of discomfort or tenderness and actual pain in the epigastrium, and sometimes in the back at the same level. Diarrhœa may be slight or absent. It is in such a condition that a catarrhal jaundice is apt to supervene, by an extension of the inflammation to the common bile-duct.

Treatment.—In the milder cases, which are of such frequent occurrence, the symptoms will often subside if the patient remains in bed for a day or two, with a diet limited to milk diluted with soda-water or lime-water; while hot fomentations to the abdomen will quickly give relief from the griping. As the diarrhœa ceases, care must be exercised in returning to a normal diet, and during the next few days broths thickened with bread crumbs, milk puddings, fish, and minced chicken may be cautiously added to the diet. In many cases, where the patient is weakly, or there is any collapse, some alcohol may be necessary. If there is clear reason to believe that the enteritis is dependent on the ingestion of some excess of food, or of some improper and indigestible material, a dose of 1 oz. of castor-oil containing 10 minims of tincture of opium for an adult, or a dose of the castor-oil mixture (B.P.) for a child, may be given with advantage when the patient first comes under observation. The pain and diarrhœa can then be dealt with by a few doses of subnitrate of bismuth, with 10 minims of tincture of opium to the dose. In younger patients, 10 gr. of aromatic chalk powder, with 2 gr. of Dover's powder, may be used with a similar effect. As a rule, no other treatment is required, as the natural tendency of an acute catarrh is towards a rapid subsidence. In those cases which are prevalent in hot weather, and which are not obviously dependent on some error of diet, it is advisable to use salicylate of bismuth and salol, 5 gr. of each. Occasionally, in the adult, there may be reason for the use of a subcutaneous injection of $\frac{1}{4}$ gr. of morphine.

In the chronic catarrh which has been mentioned as being associated with and secondary to some other disease, all drugs are often found to fail. The best remedies are bismuth subnitrate, and astringents such as dilute sulphuric acid, tincture of catechu, compound kino powder, and pernitrate of iron.

CATARRHAL ENTERITIS IN CHILDREN.

This condition is common enough in children of all ages, but is more particularly common and more grave in young children under 2 years of

age. The term dyspeptic diarrhœa, which is sometimes used, explains something of its origin. It arises largely from the improper feeding of infants, more especially of course of hand-fed infants. The feeding of infants who from some cause are deprived of the maternal nutriment is simple in principle, but requires constant care and intelligent watchfulness in practice. The actual irritant which appears for the most part to excite this enteritis in young children is either improper food, such as excess of milk, which they cannot assimilate, or starchy matter, which they are quite unable to digest, or milk which, from want of care and cleanliness, has been allowed to become a rich field for bacteria. To these causes certain conditions, such as teething and rickets, often contribute; and there is clear evidence, moreover, that the occurrence of enteritis is aided to some extent by chill, produced by improper clothing, or by sudden changes of temperature. In simple cases produced in this way, the symptoms are mainly due to the mechanical irritation of the bowel, set up by the unnatural quality or condition of the food. Such cases are, of course, more common among the poor than the rich; and they are commonly mild and easily remedied, if the child can be placed under favourable conditions. In other cases, however, there is reason to believe that the symptoms depend mainly on a bacterial intoxication, and these bacterial cases, which are of far greater severity, would probably, if our knowledge permitted, be placed under a separate heading. This form of disease is a feature of town life, and it occurs among the rich and the poor. It is particularly prevalent in hot, dry weather, and statistics show that the mortality is greatest in the months of July, August, and September.

Morbid anatomy.—There is little to add to what has already been said as to the appearances seen in the bowels of adults and older children. There is sometimes an excess of mucus, and there are often patches of hyperæmia, which are probably often a post-mortem phenomenon. There may be a little swelling of the solitary and agminated follicles, but it must be remembered that these structures are always prominent in young children. The mesenteric glands may be swollen and pink on section. The most obtrusive post-mortem evidence is given by shallow ulcers and abrasions, which are sometimes found on both solitary glands and on Peyer's patches. They are most common in the lower part of the ileum and upper part of the large intestine, but they are seen in those severe and protracted cases only which do not respond to treatment even though the apparent cause has been removed. As a result of long-continued catarrh in young children, there has been described a condition of atrophy of the glandular part of the mucous membrane, and its replacement by cellular connective tissue containing black or slate-coloured pigment. It has been already stated that a group of cases, at present included under this head, are probably in part at any rate of bacterial origin, and that the severe general symptoms which ensue are dependent on the absorption of poison developed in the intestines by bacterial life. No specific organism is known. The observations of Booker, Vaughan, Jeffries, and Baginsky point to the conclusion that many different saprophytic organisms are concerned, but that while no one variety is constant, the Proteus group, and forms closely allied to *Bacillus coli communis*, seem to predominate.

Symptoms.—In mild cases there is diarrhœa, with a frequent passage of greenish stools, which are slimy and offensive, and may show visible mucus. They have been likened to chopped spinach. If an excess

of milk is the cause, lumps of undigested casein may be recognised. The green colour of the stools is possibly due to some specific bacterial product. The child may vomit occasionally, but this is not a marked symptom. There is little or no fever, and the abdomen is soft and flaccid. The child quickly shows signs of general disturbance. He becomes pale, there is irritability and restlessness, due to pain or discomfort in the abdomen, and he frequently cries aloud. In many such cases, if they are taken in hand at an early period, appropriate dieting and treatment will bring about a cure in a few days.

In some cases, especially those occurring during hot weather, the symptoms are far more severe, or, at any rate, more rapidly attain to a high degree of severity, so that the child is already extremely ill when the physician first sees him. The symptoms here are suggestive of a bacterial intoxication, as well as of a malnutrition, induced by imperfect absorption of food from the alimentary canal. The vomiting is more frequent, the diarrhœa is more urgent, the stools contain less and less fæcal matter, and become more and more fluid, still, however, as a rule, being greenish and very offensive. Mucus is occasionally seen, but seldom in large amounts, and blood streaks may be noticed. The abdomen becomes obviously tender. It may be distended with gas, but is often shrunken and hollow. The child lies with knees drawn up and legs crossed, dreading all handling. Aphthæ may develop on the tongue and mucous membrane of the mouth. The general condition is often alarming, there is obvious wasting, and nutrition is at a standstill. The face is pinched in appearance, the eyes become hollow, and the fontanelle is depressed. The tongue grows dry, the pulse becomes rapid and feeble. The temperature, after the rule in infantile diseases, is very variable. It may quickly become subnormal, and remain so until death or recovery; or a moderate fever may set in, or the temperature may rise rapidly till a fatal termination is reached. The urine is commonly diminished in amount. At any period a collapse may set in, which can only end in death. In some instances, occurring during hot weather, collapse may set in with a suddenness and rapidity suggestive of English cholera (cholera nostras), and the distinction between the two conditions is sometimes exceedingly slight. Death may occur in three days from the onset. In other instances which are of longer duration, convulsions or broncho-pneumonia may end the scene.

There must also be described a chronic class of enteritis, which is induced by a long course of improper feeding, and is often complicated by rickets. There is either a succession of slight attacks of moderate enteritis, or there is merely a continuous slight frequency of stools, which may for a time pass almost unnoticed among unintelligent persons. The motions are commonly large, pale, soft, and pasty, with a sour, offensive smell. The child gradually grows thin, pale, and hollow-eyed. There is clearly muscular weakness. There is but little evidence of pain, and the abdomen becomes distended. The appetite is capricious; it may be voracious from time to time, but, as the mother remarks, " his food seems to do him no good." The appetite finally fails altogether. This condition is essentially one of malnutrition; and if it proves fatal, as often happens, death occurs from sheer asthenia, or from an intercurrent broncho-pneumonia or pulmonary collapse. These conditions, grouped under the name of catarrhal enteritis, and occurring in children under 2 years of age, must always engage the closest attention. The disease may, as already said, rapidly yield to dieting. It may, however, under the most favourable conditions

which can be imposed, either continue for some weeks or may become chronic. It may also prove rapidly fatal, or the child may die at a much later period from malnutrition. In any case, the main elements in prognosis are the age of the child and the previous vital condition. It is especially fatal to children who are weaned at an early period. The older the child, the greater is the resistant power, and the age of two is an important stage to be passed.

Treatment.—It happens, though but seldom, that an enteritis develops in a child which is being brought up at the breast, and in such cases it is often found that the cause lies in too frequent feeding of the child, mothers having the habit of giving the breast in order to quiet the child. In such cases a slight purgative, such as a teaspoonful of castor-oil, or two teaspoonfuls of the castor-oil mixture, or half a grain of grey powder, twice a day, with directions as to the proper method of suckling, will be all that is necessary. If there is reason to believe that the mother is supplying inferior milk, then a wet-nurse must be employed if possible.

In many cases, however, artificial feeding is a necessity. If it be carried out with care and intelligence, the fear of a catarrhal enteritis is greatly diminished. The two main objects to be aimed at in the regulation of artificial feeding of infants are—1. That the milk should approach in character as near as may be to that of the mother. 2. That it should not have undergone any degree of decomposition, and should be sterile at the time of use.

Pure cow's milk contains more proteids and more fat, but rather less carbohydrates, than human milk, its casein coagulates in large masses, which are difficult of digestion, and it is in consequence unsuitable food for a child. Pure goat's milk is hardly more suitable, for the same reason. Ass's milk, on the other hand, of which the casein coagulates in fine flocculent granules, easy of digestion, contains so small a percentage of proteids that its use cannot be maintained for long. Hence cow's milk must be used in the majority of instances. It must be assimilated to human milk by dilution, and it is found that there is less tendency to the massive coagulation of the casein when it is diluted with barley-water or with lime-water. For the first month of life the dilution should be in the proportion of one part of milk to two parts of barley-water, with the addition of a little sugar. Of this mixture 25 to 30 oz. is sufficient. The proportion of milk in the mixture may be gradually increased, and from the end of the fourth month the proportion may be as two to one, and 2½ pints may be given in the day. The milk should always be boiled, as boiling, apart from other advantages, has some effect in preventing massive coagulation of casein.

Artificial human milk may also be obtained as a commercial article, and may be found useful. The simplest plan of preparation for domestic use is that of Cheadle: "All the cream is removed by skimming after it has stood some time; then the remainder is divided into two equal portions. From one, all the casein is removed by rennet, that is, it is converted into whey; the other portion is then mixed with the whey, and the whole of the cream added. As the child grows older the proteid element should be increased by removing the curd from one-third of the milk only, instead of from one-half as at first." Such an artificial human milk, however, retains the disadvantage arising from the density of the coagulated casein.

The second object to be kept in view in the feeding of infants is

cleanliness. The milk must be as fresh as possible; it must always be boiled, or at any rate sterilised, and the bottle and all its parts must be kept perfectly clean.

If these principles be observed in the feeding of infants, the frequency of a catarrhal enteritis will be greatly reduced, and a return to these principles, if they have been departed from, is sometimes the only treatment required. The removal of the child from a town to a bracing country air is an important preventive measure, and it is equally important during convalescence.

When, however, the symptoms are more severe, additional treatment and a special diet will be required. All milk should be at once forbidden, and proteid material must be given in other forms. The white of an egg stirred up in half a pint of water, with a few drops of brandy and a little salt, is a good article of diet. Veal or chicken-broth may be used. Raw-meat juice is often readily taken. It may be made by finely mincing some beefsteak, soaking it in a little cold water, and then expressing the juice, either with a lemon squeezer, or by forcibly twisting it in muslin. Of this 2 or 3 oz. may be given in twenty-four hours. Raw meat may also be used with advantage for children from 8 to 12 months old. It is made by scraping the best steak into a pulp, pounding in a mortar, and straining through a fine sieve; 2 oz. may be given in twenty-four hours, and it is well to add to it and to the meat juice a little salt. These forms of food may be combined or alternated according to circumstances. Alcohol is often necessary, and half an ounce in the twenty-four hours may, during a period of emergency, be safely given to a child of 3 months old. Barley-water may be given freely for thirst; whey is often useful, and is well taken, and if there is any sign of exhaustion, it is a good vehicle for the administration of alcohol. The abdomen and extremities must be kept warm, and if the temperature is high, it should be reduced by tepid bathing. Food must be given in small quantities, and should be cold; it may be given at intervals of two hours. If the child is seen at an early period, it is advisable to give an aperient such as a teaspoonful of castor-oil, or two teaspoonfuls of the castor-oil mixture. For this, if the vomiting is urgent, a powder may be substituted, containing 3 gr. of powdered rhubarb and 2 gr. of bicarbonate of soda; and this may be followed with advantage, in cases where the diarrhœa is not very severe, by half a grain of mercury and chalk, with half a grain of Dover's powder, given twice a day for two or three days, in the case of a child of 6 months old and upwards.

If the diarrhœa is more urgent, and the drain of fluid and risk of exhaustion is great, it must be dealt with energetically by the use of subnitrate of bismuth, Dover's powder, and aromatic chalk powder. If the vomiting is persistent, powders are preferable to liquid medicine. Five gr. of subnitrate of bismuth with a quarter of a grain of Dover's powder, and 3 gr. of aromatic chalk powder, may be given every four hours to a child 6 months old. In a fluid mixture containing the same amount of bismuth, half a minim of tincture of opium may be used. The dose of Dover's powder and of tincture of opium may be doubled for a child of 1 year. In some of these cases, at any rate, especially those occurring in hot weather, there is distinct indication for the use of some intestinal disinfectant. It is, however, by no means clear that any of the drugs which can be used for this purpose, such as β-naphthol, resorcin, perchloride of mercury, salol, etc., can be trusted to give a better result than the bismuth

mixture above mentioned.   Three gr. of salicylate of soda or one-eighth of a grain of calomel, may however, be given with the bismuth every four hours to a child 1 year old, or a powder containing 3 gr. of salicylate of bismuth with 2 gr. of salol may be used with advantage.   When the process of exhaustion is proceeding apace, infusion with normal saline solution is of great service, as in the choleraic form of diarrhœa, which is subsequently described.

In chronic cases the same lines of dietetic and medicinal treatment must be observed.   There must be great caution in the return to a milk diet, and quinine and acid tonics will be useful during convalescence.

CHOLERA NOSTRAS.

This is an acute disease, occurring in temperate climates, which has a close resemblance to Asiatic cholera, but differs from it in being of sporadic, not endemic, occurrence, and in being milder and far more favourable, at any rate in adults.   It is common enough in the adult; but is especially apt to attack children, and in them has a high rate of mortality.   It is almost confined in its occurrence to the hot months of the year, and becomes most common when heat and drought are combined. It has been shown that it is particularly apt to occur when the temperature of the earth at a depth of 1 foot reaches 62° F. (Tomkins.)   In some cases, especially in adults, there is a history of having eaten some article which is prone to decomposition, such as sausage-meat, and shellfish, but in many instances no such history is forthcoming.

Morbid anatomy. — The rapid development of such severe symptoms, the absence of evidence of gross structural disease in the intestine, and the close resemblance to Asiatic cholera, point strongly to the cause as being the absorption of some poison of bacterial origin from the alimentary canal, either taken in from without, or more probably produced there by bacterial action.   The spirillum of Finkler and Prior, which has been advanced as the cause, is now discredited.   No specific organism is known ; and the evidence at present to hand points rather to the agency of some one or more species of common putrefactive organism, such as *Proteus vulgaris* and certain allied forms.   Post-mortem changes are exceedingly slight.   The stomach and intestines are usually empty and pale. There may be patches of hyperæmia in the small bowel, and occasionally punctiform hæmorrhages may be seen in the mucous membrane.

Symptoms.—The patient is suddenly seized with vomiting and diarrhœa.   After the preliminary rejection of the contents of the stomach, copious vomiting of fluid continues, which is to a less and less extent tinged with bile.   The motions are similarly at first bile-stained ; but they become more and more colourless, and may reach the rice-water condition of Asiatic cholera.   They are often exceedingly profuse; there may be a large outpouring of fluid every hour, with pain and griping.   Sometimes the abdominal pain is very slight.   There is always great thirst, and there may be severe cramps in the muscles of the limbs, especially in the calves.   The collapse is rapid and alarming, the pulse becomes quick and feeble, and the temperature is subnormal.   The eyes are sunken, the extremities feel cold and have a bluish tint ; the skin of the fingers becomes wrinkled, as if the tissues were shrunken.   The urine is scanty or entirely suppressed.   In this condition the patient may remain for twenty-four or thirty-six hours, and it is in this stage that death, if it occurs at all, supervenes.   If this stage is

survived there is little further danger to be apprehended. The vomiting and diarrhœa subside, the collapse passes off, and the recovery is strikingly rapid, considering the extremity of the illness so quickly reached, and it is usually complete in three or four days. Not all cases are so severe as in the example here given. Milder forms occur, and in this direction the disease shades off into the severer forms of catarrhal enteritis previously described, and no accurate line of demarcation is possible. The stools in all cases should be examined with a view to determining the presence or absence of comma bacilli; but expert knowledge is required for the purpose. A fatal event is by no means common. It is more likely to occur in the old or feeble, or in those debilitated by alcohol or previous disease; but it may undoubtedly prove fatal even in the physically strong and healthy. In children, however, it is attended with a high rate of mortality.

Treatment.—The administration of drugs by the mouth or by the rectum in the early stage is difficult or impossible, owing to the incessant vomiting and diarrhœa. And the subcutaneous injection of morphine, freely but carefully used, is often the only remedy, and even this must be discontinued if the patient becomes collapsed and the urinary secretion much diminished. If the vomiting is not very urgent, salicylate of bismuth and salol with Dover's powder or tincture of opium may be administered from the first. Iced brandy and water may be given in small quantities, and some may be absorbed even in severe cases, or iced milk or barley-water with brandy or whisky in it. Hot fomentations, with or without mustard to the abdomen, undoubtedly give relief. If the collapse is severe, the patient must be infused with normal saline solution, and four or five pints at least may be allowed to run into a vein in the arm, with a marvellous effect upon the condition and appearance of the patient. Inasmuch as the period of collapse is a short one, one infusion may prove sufficient; but it may always be safely repeated, though the success attending second and subsequent infusion is much less marked than that of the first. Large enemata of water, given by gravity, up to two or three pints, will certainly prove of service, but a profuse diarrhœa will hinder their use. As soon as the diarrhœa and vomiting begin to abate, there is little cause for further anxiety, and the feeding may be steadily increased on general principles without fear of relapse.

CHOLERA INFANTUM.

We have here to deal with an affection which is probably identical with the cholera nostras already described. It is common among children in large towns during the hot months of the year, and it annually claims so large a number of victims that it merits some separate description. As regards its causation and nature nothing need be added. That its symptoms are dependent on the absorption of a bacterial poison, and not upon any gross intestinal change, is rendered probable by the evidence already given as regards cholera nostras, and it must be admitted that no absolute line of demarcation can be drawn upon clinical grounds between it and the more severe form of catarrhal enteritis already described.

Morbid anatomy.—The absence of post-mortem changes after such a rapid and violent death as may occur is very striking. The intestines are pale and shrunken and translucent, and seldom show any hyperæmia, or at most patches of injected vessels which are not improbably a post-

mortem phenomenon. No change, or at most only a little swelling, is to be observed in the lymphatic structures. All the tissues, especially the serous membranes, are unusually dry, and the organs are very pale.

Symptoms.—The illness has commonly a rapid and violent onset. The child is seized with vomiting and diarrhœa, both of which become violent and incessant. The vomit becomes a watery bile-tinged fluid. The stools soon lose all trace of fæcal matter, and have but little smell. They consist of a thin serous fluid, which may be colourless or but little tinged with bile. A stool may be passed every hour. There is usually great restlessness at first, and probably also pain and aching in the limbs. The child's thirst is distressing, and it cannot be appeased, owing to the vomiting. There is a rapid alteration in the child's appearance. In a few hours the eyes may be sunken, the face deadly pale, with cheeks fallen in, and features sharpened. The fontanelle becomes depressed, the abdomen shrunken and flaccid, the tongue dry, the pulse small, frequent, running, and uncountable. The temperature in the axilla at any rate is usually subnormal, and may fall to 96° or lower before death, but the rectal temperature is often found to be raised, and may reach 104°. The urine is necessarily scanty, or is completely suppressed. In cases that are going to prove fatal, the restlessness passes into apathy, drowsiness, and apparent peace. Sometimes convulsions end the scene. Some cases, of course, end favourably, but death is the more common ending, and it may occur in the first day of the illness, or life may be prolonged for three or four days.

Treatment.—The disease must be combated energetically from the first, if the child is to have a chance of living; but as in Asiatic cholera, so here, the administration of any food or medicine by mouth or rectum is difficult or impossible.

As regards feeding, in severe cases it is impossible to administer nutriment. When, however, the vomiting is less urgent, persistent efforts should be made to introduce nutriment into the stomach. Milk is out of the question. Small quantities of whey with alcohol or iced champagne, or raw-meat juice give the best chance, and plenty of iced barley-water may be allowed, or water containing the whites of two eggs, and 1 oz. of brandy to the pint may be used. An attempt may be made also to administer alcohol and strong beef-tea by the rectum, and possibly some may be absorbed between the stools. Hot baths are of decided use, containing 1 oz. of mustard to the gallon. Injections of brandy under the skin are of use in tiding over the acute period, and there is no doubt as to the value of large intravenous infusion of saline fluid, though the good effect is but of short duration, and can hardly be attained by its repetition. As regards drugs, morphine subcutaneously stands in the front rank. A child of one year old may safely have one-fiftieth or one-thirtieth of a grain at intervals of two hours, but as regards the numerous other drugs, the so-called intestinal disinfectants, such as salol, perchloride of mercury, resorcin, etc., the incessant vomiting as a rule will not admit their use. Large rectal injections of iced water have been found of service. If the symptoms show signs of subsiding, the field for food and drugs is wider. Still keeping to alcohol, beef-juice, whey, or brandy-and-egg mixture, opium (as the tincture or as Dover's powder) may be administered by the mouth. And as recovery ensues, the feeding must be carefully increased, but milk must be withheld until some time after all danger is over. If the fever is high, baths may be used, but this is seldom an urgent symptom. It must be

remembered in the treatment that it must be assiduous and energetic from the very first, and that attention must be more particularly directed to preserving strength for the three or four days of danger.

CROUPOUS OR DIPHTHERITIC ENTERITIS.

An inflammatory disease of the bowel, which is characterised by some degree of necrosis of the mucous membrane, and by the formation of a pellicle consisting of coagulated exudation. The old-fashioned term diphtheritic has reference merely to the formation of a membrane as characterising the disease, and it does not imply any theory as to its origin.

Etiology.—The actual origin of this form of enteritis is unknown. It is occasionally found unexpectedly in the post-mortem room, after death from severe bacterial or chronic diseases, more especially pneumonia, pyæmia, typhoid fever, cirrhosis of the liver, and Bright's disease. It may be set up by the action of certain poisons, such as mercury, arsenic, and lead. It also occurs, though rarely, as a primary disorder of the bowel, independent of disease elsewhere.

Morbid anatomy.— The main changes are a necrosis of the mucous membrane and the formation of a membrane on the necrosed area, which consists of coagulated inflammatory exudation. The necrosis may be superficial, or it may involve the whole thickness of the mucosa. The grey patches thus formed are found at any part of the intestine, large or small. They are apt to occur on prominent points of the mucous membrane, such as the valvulæ conniventes or the intersaccular ridges of the colon. Sometimes the solitary follicles are more particularly affected. Sometimes a few large patches are found, and in the case which is mentioned below as being of primary occurrence one large patch 4 in. by 2 in. occupied the sigmoid flexure, the rest of the intestine being healthy. There is usually some affection of the rest of the bowel wall at the affected point. The membranous patch is surrounded by a zone of hyperæmia, the submucosa and muscular coats are swollen and œdematous, and sometimes the whole thickness of the wall has been found in the post-mortem room to be gangrenous or of doubtful vitality. It is probable, from the analogy of membranes of similar structure elsewhere, that the immediate origin of the croupous inflammation is to be sought for in bacterial agency.

Symptoms.—No detailed account of the symptoms of this condition can be given. It is sufficient to say that it is most commonly marked by profuse diarrhœa, which is scarcely controlled by any drugs, and occasionally by the passage of blood. Pain is commonly absent. It arises for the most part, as has been already said, in a late stage of other diseases, so that any special characters it may have are necessarily obscured.

On the other hand, the primary form of the disease may bear a close resemblance to intestinal obstruction or peritonitis. There is complete constipation, though flatus may be passed. The vomiting is severe, the tongue becomes dry, the pulse rapid, and the abdomen becomes distended and often tender. The constipation is presumably due to the paralysis of a large section of the bowel. In one such case the patient was seized with violent abdominal pain, vomiting, and rapid collapse, which suggested an intestinal obstruction, and abdominal

exploration was carried out on that supposition. Death occurred within forty-eight hours of the apparent onset.

Treatment.—The treatment in the commoner form of the disease must be by drugs such as have been already recommended in the case of the chronic catarrhal form of enteritis, which arises under somewhat similar conditions; and if the general condition of the patient permits it, an attempt may be made to control the diarrhœa by large astringent injections of alum, sulphate of copper, or nitrate of silver.

PHLEGMONOUS ENTERITIS.

This condition is rarely if ever a primary occurrence. It results usually from some severe mechanical damage to the bowel, such as may be caused by an intussusception, by strangulation of the bowel in the abdominal cavity or in the hernial apertures, and by the impaction of a gallstone. All the coats of the bowel are implicated at the damaged spot. The peritoneal surface is dark red or purple, or even black. Its polish may be lost, and it may be sticky, or roughened by a deposit of coagulated inflammatory exudation upon it. The other coats are swollen and soft, owing to their congestion and œdema, and in some cases they become gangrenous. The condition is very severe. Pain, vomiting, complete inaction of the bowels, abdominal distension with fever and collapse, are the salient features. The symptoms closely resemble those of peritonitis, and indeed some degree of peritonitis is commonly associated. The medical treatment must be such as is laid down for peritonitis, but it is commonly of little avail, and the resources of surgery, if timely, may afford some hope.

MUCOUS COLITIS.

An affection which is probably limited to the large intestine, and is characterised clinically by the passage of much mucus in the stools. The mucus often occurs in the form of membranous casts of the bowels (*entérite muco-membraneuse*), but the disease must be carefully distinguished from the croupous or diphtheritic enteritis already described.

Etiology.—Our knowledge of its causation is scanty. It occurs most commonly in adults between the ages of 20 and 40, but is occasionally met with outside these limits. It is far more common in women than in men, the proportion being roughly as four to one. Both the men and the women who are affected seem to be of a peculiar temperament; they are nervous, excitable, and unstable, with a tendency to neurasthenia. In late stages they often become hypochondriacal and even melancholic. The neurasthenic tendency seems to be a constant and early accompaniment, and to this extent heredity plays some part. It is almost invariably accompanied by chronic constipation, but this can hardly be taken to have a very close connection with its origin, if the relative frequency of the two conditions is compared. There is no evidence pointing to any bacterial agency. It has often been noted to occur in association with disease of the vermiform appendix.

Morbid anatomy.—Nothing certain is known as to the pathology of the disease. An inflammatory process in the bowel wall has been described, but, considering the long duration of the disease, it is improbable that there is any gross structural change in the majority of cases. The membrane has indeed been seen *in situ*, closely adherent in the colon, and

it was capable of separation without any lesion of the surface (Osler). It is possible that it is essentially a disturbance of secretion, independent of any inflammatory process, and in support of this view it should be noted that the disease is almost confined to the neurasthenic stock, and that the amount of mucus produced is far greater than in any known form of definite inflammation of the bowel.

Symptoms.—It is not a common affection in this country, but it seems to occur more commonly in private than in hospital practice. In well-marked cases the disease runs a course of many years. There are definite attacks of abdominal pain with the passage of mucus, and between the attacks the patient may enjoy fair health although usually constipated. The attacks last for a week or more, and they recur at variable intervals. Sometimes a succession of attacks may occur with hardly any interval, sometimes there are only two or three in a year. The pain is of a colicky griping nature, and may be severe. It may be referred by the patient to either side of the abdomen, and is often referred to one or other of the iliac fossæ. There is usually a general feeling of illness; there is sometimes nausea, and occasionally vomiting. The temperature is rarely if ever raised. The abdomen is often somewhat distended, and it presents some tenderness on palpation in some part of the course of the large intestine. After one or more days spent in this condition, during which the patient is commonly confined to bed, the constipation yields to some extent, and with every stool there is passed a notable quantity of mucus. The mucus may appear in flakes, round masses, or strings, but it often forms a complete cast of the bowel from an inch to a foot in length. These casts, of which the tubular character is seen, if they are unfolded under water, are tough and somewhat translucent, and may be one-eighth of an inch in thickness. Chemically they may be shown to consist of mucus, but they contain also degenerate epithelial cells, fæcal particles, and phosphatic crystals. No fibrin enters into their structure, but they may contain a small quantity of some proteid substance. Rarely they have been seen to be streaked with blood. Mucus in one or other form may thus be passed once or several times a day for several days, when it disappears. The pain then subsides, and the patient returns to comparative health.

During the intervals, however, constipation is always troublesome. The patient is, moreover, apprehensive of the next attack. She is dyspeptic, anæmic, and ill-nourished. There is a tendency to depression, with loss of energy and loss of interest in surroundings, but this mental condition seems rarely to pass the boundary line into actual melancholia.

Not all instances have so sharp an outline as this, though the general characters described above can always be recognised. Sometimes the habitual constipation is the salient feature, and the attacks of mucus-passing and pain may be ill-defined and may pass unrecognised. On the other hand, exceptional cases have been recorded, in which the attacks have been severe and continuous, and mucus has been passed in great abundance with diarrhœa, and a fatal event has occurred apparently through sheer exhaustion. It should be noted that the paroxysmal attacks may bear some resemblance to attacks of local peritonitis arising round a diseased appendix, especially when the pain and tenderness are limited to the right iliac fossa. The distinction between the two conditions can be readily made at the time of the attack, by the absence of fever and of any definite sign of peritonitis, but the differential diagnosis may be very

difficult in the interval, when an actual attack has not been closely observed, and it can be made only by a careful sifting of the history.

The duration of the disease cannot be stated with accuracy. It certainly may disappear, though this result can be hardly attributed to any particular course of treatment. But more commonly it continues unchecked for many years.

Treatment.—In the present state of our knowledge the treatment of this disorder can only be tentative. For the general condition, especially if there is wasting, a course of general massage may be found to be of some use, and arsenic or strychnia may be administered at the same time. Iron can hardly be used without increasing the constipation. Salicylate of bismuth or salol, or both, are often used and may have some effect in diminishing the frequency of the attacks. The diet must be simple and plentiful, but there is no reason for choosing one form of food more than another. The life must be as regular and healthy as circumstances allow, and the surroundings should be bright and cheerful. The constipation must be treated on general principles, such as are laid down elsewhere, and strong purgatives are to be avoided.

During an attack the pain must be relieved as far as possible by hot fomentations and counter-irritants. Morphine should never be used, as all the conditions are present which favour the development of a morphine habit. Cannabis indica has been recommended as a substitute. The diet should be limited to milk. The castor-oil mixture is of use in aiding the expulsion of the mucus, and large injections of warm boracic acid solution, gently administered by gravity, may possibly be of service. No specific cure is known, and cases are rare in which any improvement can be truly attributed to any particular method of treatment.

It has been suggested that in severe cases, where the patient is showing signs of exhaustion, owing to a continuance of painful attacks, it may be justifiable to make an artificial anus into the ascending colon, with the double object of affording rest to the lower bowel and of being enabled to flush it out thoroughly from above. A case of this kind under the care of Hale White was followed by a fair measure of success.

ULCERATIVE COLITIS.

This name is given to an ulceration of the colon, which occurs in temperate climates. The naked-eye characters of the bowel closely resemble those of dysentery, but the clinical features of the two conditions present some points of difference.

Etiology.—No specific cause is known, and no connection has as yet been traced with any protozoon or microbe. It has no apparent relation with locality, season, or climatic condition. It occurs in both sexes, perhaps rather more commonly in women than men, and attacks adults of any age. There is some evidence as to a late association with chronic interstitial nephritis and gout.

Morbid anatomy.—The appearance of the colon after death is much the same as in dysentery. The ulceration may be found in the whole length of the large bowel, or it may be limited to a portion of it, a foot or so in length, or it may occur in separate patches. Usually there has been great destruction of the mucosa and submucosa, so that the muscular coat is laid bare in the floor of large ulcers. The ulcers are of various sizes and shapes, sometimes separate, sometimes confluent. The surviving

mucous membrane is represented by islands of œdematous tissue, which are often undermined at their bases, and are therefore polypoidal in shape. Strands of surviving mucous membrane may also be seen, which are completely undermined and left as bridges over an ulcer. If larger tracts of mucous membrane remain, there may be seen small orifices in it, which have given exit to inflammatory products from below. A similar appearance is seen in amœbic dysentery (Councilman and Lafleur). And these appearances may perhaps be taken as indicating that the deeper part of the mucosa or the submucosa is the starting-point of the morbid change.

Symptoms. — The chief feature of the disease is an intractable diarrhœa. The bowels are moved at least three or four times in the day, sometimes much more frequently. The motions commonly consist of a little fæcal matter unformed, with dark offensive fluid, and they often contain blood. Sometimes in later stages the hæmorrhage may be severe, and it has been known to be the immediate cause of death. Mucus is not present, except perhaps in an early stage. There is seldom any severe rectal pain or tenesmus, but there is often considerable general pain in the abdomen, both during defæcation and at other times. Sometimes, however, it is slight and unimportant. Vomiting is uncommon. The tongue is pale and furred, and may become dry. The temperature may be normal throughout, but there is sometimes a moderate degree of pyrexia, and an evening record of 104° is occasionally reached. The abdomen may be flaccid or slightly distended, and, owing to the thinness of its wall, the peristaltic movements of the intestine may sometimes be seen. The patient wastes rapidly, and an extreme degree of emaciation may be reached, if life be prolonged. Hepatic abscess may conceivably occur, as in any ulcerative condition of the bowel, but it is very rare. Death commonly occurs from exhaustion, but sometimes by perforation and peritonitis. The duration of the acute disease is seldom more than two months, and it is almost invariably fatal. In some instances, however, it has been known to undergo temporary abatement from time to time, so that it has extended over a year or more, but it is doubtful whether permanent recovery ever occurs.

Treatment.—No specific cure is known. The treatment is much the same as is suggested for a chronic dysentery. Absolute rest, with a milk diet, must be obtained. Bismuth and opium will probably afford as much relief as can be expected in so severe a condition, and the propriety of making an artificial anus in the ascending colon, in cases which are not too far advanced, must always receive consideration.

INTESTINAL OBSTRUCTION.

The conditions here described will be seen to arise from widely different causes, but they have one common feature, in that they all produce some mechanical impediment to the passage of the intestinal contents. In many of these conditions some damage is inflicted upon the bowel wall at the same time. The combined symptoms, which result from the mechanical impediment and from the damage to the bowel, vary from those of a mere chronic constipation to those of an acute attack, terminating fatally in a few days. These conditions are commonly arranged under the following heads :—(1) Strangulation by bands or through

apertures, (2) stricture, (3) volvulus, (4) compression and traction by adhesions, (5) intussusception, and (6) blocking by foreign bodies.

Etiology and pathology.—Strangulation by bands or through apertures.—This is the most common form, and roughly one-third of all cases of intestinal obstruction fall under this head. The type of the group is the strangulated hernia, which is dealt with in surgical text-books. The mechanism of strangulation of the bowel is the same in all instances. It may be broadly stated that a loop of the bowel, usually the small bowel, is thrust by some sudden movement through an aperture, which is sufficiently narrow or tight to obstruct the venous flow from the portion engaged. The swelling of the loop, which immediately ensues from the venous engorgement, hinders its return, and in nearly all cases its release quickly becomes improbable, save by surgical aid. The bowel is then said to be strangulated. The interference with the blood supply of the affected part may be so extreme as to lead to gangrene.

The aperture is in most cases formed by the stretching of a band in some part of the abdomen, either from bowel to bowel, or more commonly from bowel to some part of the abdominal wall, or to the omentum, or to some viscus, such as the uterus. Such a band is commonly an elongated adhesion, which is a relic of a previous peritonitis. Sometimes, especially in the young, it consists of Meckel's diverticulum, the tip of which has become adherent to some part of the peritoneal surface. Less commonly the vermiform appendix or the Fallopian tube may be the cause. An omentum which has become adherent at some point of its free edge may become in whole or in part rolled up and sufficiently cord-like to produce obstruction. Such a condition of the omentum may be met with in association with long-standing femoral or inguinal hernia. The pedicle of an ovarian or uterine tumour may act in the same way. Besides such a passage of the bowel under a band, it may become strangulated by passing through a slit, sometimes present in omentum or mesentery as a congenital defect, or perhaps as a result of injury. Diaphragmatic and obturator hernia must be borne in mind, as well as the rare occurrence of hernia into various pouches of the peritoneum. The forms of obstruction included in this class occur more commonly in males than females, the proportion being as three to two. It is most common between the ages of 20 and 40. Cases may occur at any time of life, and strangulation by Meckel's diverticulum is not uncommon in childhood.

Stricture.—Under this head are included all cases of narrowing of the bowel, due to changes in its walls. These changes are either of the nature of cicatricial contraction or of new growth.

The cicatricial form is by no means common. It may possibly arise from a tuberculous ulcer, but the healing of such an ulcer is exceedingly rare. It is improbable that narrowing of the bowel ever arises from a typhoid ulcer. It occurs in the rectum from the cicatrisation of syphilitic ulceration, and in the large bowel as a result of dysentery. In the small bowel the most common form of stricture is that produced by the healing of an ulcer which is of unknown origin. Many instances have been recorded of this solitary ulcer, and in not a few the first symptoms have been produced by the narrowing consequent upon its healing. It is most common low down in the ileum, and is possibly of syphilitic origin. Rare cases have been recorded where the incarceration of a loop of small bowel in a hernia has set up cicatricial changes in its wall, which have led

to obstruction at a later period. Still more rarely the same result has followed an injury. The stricture of the duodenum, which may result from a solitary ulcer, is better considered in relation to diseases of the pylorus. Congenital narrowing or occlusion of the bowel belongs to the department of the surgeon.

The malignant stricture, on the other hand, is exceedingly common. The new growth which produces it is nearly always a primary one, the almost universal form of the growth is a columnar-celled epithelioma, and its seat is nearly always in the large bowel, most commonly in the rectum, or sigmoid flexure, or lower part of descending colon; less commonly at the ileo-cæcal valve, or at the hepatic or splenic flexures. The growth has a tendency to surround the bowel in annular fashion, so that it may produce a high degree of obstruction even in an early stage, and there is often a considerable development of fibrous tissue in it, which tends by its contractile tendency to increase the narrowing of the bowel. This form of growth is usually met with after middle life, but it has been known to occur at the age of 20. Simple tumours, such as adenomata, fibromata, and papillomata are also occasionally met with in both large and small intestine as the cause of obstruction, but their occurrence is not of sufficient frequency to require their consideration at the bedside.

Volvulus.—A twisting of the bowel upon itself, so as to lead to strangulation, is far more common in the sigmoid flexure than elsewhere, owing to its long mesocolon and comparative freedom of movement. It leads to enormous dilatation of the bowel, the affected part possibly filling two-thirds of the abdomen. There is great congestion. It becomes purple or black and gangrenous. Blood is commonly extravasated into the interior, and some degree of peritonitis is quickly developed. The same accident may happen to the cæcum, especially when an unusual amount of it has no mesenteric attachment. It is simply twisted upon itself to the left, and a turn through a right angle may be sufficient to cause strangulation. It has been found also to be bent upwards upon itself, the caput cæci lying on the ascending colon. More rarely the volvulus affects the small bowel, and occasionally two loops of small bowel have become twisted round each other. It is more common in males than females, and it seldom occurs before middle life. As regards the sigmoid flexure, it is closely connected with habitual constipation.

Compression or traction by adhesions or tumours.—This large group of conditions is a fertile source of intestinal obstruction. As a result of peritonitis, the small bowel may become matted and adherent, coil to coil, to a variable extent. An extreme degree of this matting is sometimes met with in cases of chronic peritonitis, which are usually of tuberculous origin. The whole of the small bowel from duodenum to cæcum may be gathered up into a coherent mass, which defies dissection in the post-mortem room. A minor, though equally fatal, degree of the same condition is found after repeated attacks of appendicular peritonitis, and such coils as lie in the right iliac fossa become inextricably welded together. The same result may follow pelvic peritonitis in women. It may also follow the slight damage to the peritoneum, which is necessarily inflicted during abdominal operations, such as the removal of the uterine appendages or an ovarian tumour; and the symptoms of obstruction have been known to supervene some months or even years after such an operation. All degrees of this condition are met with, from a matting of the whole length of the small bowel to an adhesion of the opposed surfaces of a single loop,

such as is sometimes found after the release of a strangulated hernia. In all these examples the lumen of the affected bowel may remain of considerable size, but the obstruction arises partly from the interference with or complete prevention of peristalsis, partly from the fixation of the bowel in a bent position, and sometimes from a definite compression to which the bowel is subjected by cicatricial tissue developed in and around its peritoneal coat.

Obstruction may equally result when a portion of the bowel is fixed by adhesion to some part of the abdominal wall, especially the pelvic wall, or to some viscus, such as uterus or bladder, or to a new growth, such as an ovarian or uterine tumour. The length of bowel so fixed may be extremely small. Such cases may arise after the release of a strangulated and inflamed hernia. An adhesion of one inch of the small bowel to the fundus of the uterus has proved fatal five years after a successful operation for the release of a strangulated inguinal hernia. The small bowel may also acquire a local adhesion to a tuberculous mesenteric gland. The same result may follow from any form of peritonitis, and it is not uncommon around the appendix and Fallopian tube.

An adhesion sufficient to produce fatal obstruction is not necessarily of long standing. Delicate organising adhesions may set up the symptoms of obstruction within ten days or even less after an abdominal operation. They are more particularly formed around a raw surface, such as a stump of omentum or the pedicle of an ovarian tumour, and they may necessitate a reopening of the abdominal cavity. There is in such cases a hindrance to peristalsis and perhaps some narrowing of the bowel, but the obstruction is in great measure due to some degree of kinking of the bowel at the point of fixation. An acute and impermeable kink may be caused also by the traction of a band, or of an adherent Meckel's diverticulum upon any portion of the bowel. The bowel, small or large, may also be compressed by an abdominal tumour. More especially does this occur in the pelvis, owing to the comparatively narrow space with bony walls and the frequency of large firm tumours in this situation.

Intussusception.—If from any cause one portion of the bowel slips into the part immediately below it, an intussusception is said to result. It can be readily understood that on making a section across the bowel at the affected spot three layers will be met with, namely, externally a receiving layer, internally an entering layer, and between these two a middle or returning layer, of which the peritoneal surface is apposed to the peritoneal surface of the entering layer. The direction of the intussusception is always downwards; that is, it follows the course of the intestinal contents. It tends to increase steadily, the increase being at the expense of the outer layer, so that the head of the advancing intussusceptum remains unaltered. When only an inch or two of the bowel is thus engaged, the obstruction may be very slight, and the symptoms may be obscure. But as the intussusception increases in extent, the mesentery which enters with the bowel into the receiving layer tends, from its mode of attachment, to pull upon the intussusceptum, so that its orifice no longer faces downwards in the axis of the receiving bowel, but is apposed to its side. And the obstruction is further increased by the extreme congestion and swelling of the intussusceptum, which results from interference with its venous circulation.

An intussusception may occur anywhere in small or large bowel, but for practical clinical purposes the condition may be considered to be

confined to the neighbourhood of the ileo-cæcal valve. In most cases (the ileo-cæcal variety) the valve passes into the cæcum and colon, and remains the head of the advancing intussusceptum. In rare cases (the ileo-colic variety) the ileum is protruded through the valve. The portion of bowel affected forms a thick sausage-like tumour, which may be from 2 to 6 in. in length, situated at first in the right half of the abdomen. The tumour, if sufficiently elongated, usually shows a curved shape, with the concavity downwards and to the left, this shape being impressed upon it by the course of the colon and by the attachments of the mesentery. The intussusceptum may travel so far along the large intestine that the valve may be felt in the rectum, or may even protrude at the anus.

The return of the entering part of the bowel is hindered at first by the œdematous swelling which results from the pressure on its veins, and at a later stage by inflammation of the apposed peritoneal surfaces of the entering and middle layers. The congestion of the intussusceptum is often extreme. It becomes livid or black, and there is commonly some hæmorrhage, both into the lumen of the bowel and into the space between the middle and receiving layers. The interference with the blood supply is occasionally so extreme that sloughing of the intussusceptum may result, and cases have been recorded where such sloughing *en masse* of the intussusceptum has occurred, and, union having been previously effected between the entering layer and the point of junction of middle and outer layers, the lumen has been thereby restored, and a natural cure has followed. No such fortunate result, however, can be anticipated in actual practice.

Statistics show that intussusception forms about one-third of all forms of obstruction. It is more common in males than females. It occurs especially in children. It may be met with in infants. A large proportion of cases occur during the first year, and more than half in the first decade of life. The children are usually strong and healthy, and often no cause for intussusception can be found. In many cases it seems to follow diarrhœa; in other cases a history of constipation is obtained. It is probable that the actual starting-point is an irregular peristalsis, which results in the sudden drawing up by the longitudinal muscle of one section of the bowel over another. And its production is aided by unusual mobility and size of the colon. When an intussusception is once formed, its steady increase and downward passage is readily understood, if it is looked upon as a foreign body, which is grasped and passed onwards by the receiving bowel. In some few cases a polypus or carcinomatous tumour, especially an epithelioma of the cæcum, has been found to be the head of the intussusceptum, and to have led to its formation.

Foreign bodies.—A foreign body taken in by the mouth is rarely found to be the cause of obstruction, since the bodies that can pass down the œsophagus can usually also pass through the bowel, and large bodies, such as marbles, coins, and buttons, are commonly swallowed by children without any ill effect. In rare cases, so rare as hardly to enter into clinical consideration, foreign bodies, such as coins and false teeth, have become impacted in the bowel. Rather more commonly, fruit stones, which have been swallowed in numbers, have set up obstruction. They may accumulate in the sigmoid flexure, and may form, with inspissated fæcal matter, a hard obstructive mass. It has happened that the reckless use of large quantities of insoluble salts, such as those of magnesium and bismuth,

has resulted in the formation of concretions. A much more common foreign body is a large gallstone. This source of obstruction is of sufficient frequency to demand consideration at the bedside. It usually occurs late in life, and is rare before the age of 50. The stone commonly enters the small intestine, not by the common bile duct, but by ulceration through the wall of an adherent gall bladder, and it is apt to be arrested at the ileo-cæcal valve. Fæcal impaction will be considered in relation with chronic constipation.

General effects upon the bowel.—In general, the bowel below the seat of obstruction is pale, collapsed, and empty. The bowel above is distended, injected, and full of fluid contents. If the obstruction has been of long standing, as in carcinoma of the colon, the portion above, for 6 in. or more, shows some thickening, due to hypertrophy of the muscular coats. In the case of a volvulus of the sigmoid flexure, the loop of bowel becomes enormously distended, and may come to fill a large part of the abdomen. In all cases where some degree of obstruction has been present for periods of more than two weeks, there is a tendency to ulceration of the bowel above the site of obstruction. When the obstruction is in the large bowel, even in the sigmoid flexure or rectum, it is noteworthy that the ulceration is usually limited to the cæcum, and here there may be found one or more deep punched-out ulcers. When the obstruction is in the small bowel, and especially when it is due to stricture about the ileo-cæcal valve, or to adhesions around the lower part of the ileum, the distended part of the ileum may show numbers of ulcers distributed, perhaps, over several feet of the bowel. These ulcers may be seen to arise usually in the solitary follicles. One or more of these ulcers, whether in the large or small bowel, may give way during life, and set up a fatal peritonitis. Further, there is a tendency in a later stage, especially in obstruction by strangulation, or by volvulus, for the development of some degree of peritonitis at the seat of the disease, owing to the damage inflicted upon the bowel.

Finally, it must be remembered that the symptoms of actual obstruction are often of sudden occurrence, though the cause of the obstruction, such as a carcinoma of the sigmoid flexure, has been in existence for many months. This must usually be attributed to the impaction of fæces in the narrowed bowel.

Symptoms.—There are certain cardinal symptoms by which the occurrence of intestinal obstruction is to be recognised. They are common to all forms. (1) Pain is nearly always a marked feature. It may be very severe and sudden in its onset in cases of such violent nature as strangulation, volvulus, and intussusception. It is less severe in cases of more gradual onset, such as are due to adhesions and stricture; and in some cases it may scarcely be complained of, though it is never absent. The nature of the pain is important. It differs from that of peritonitis in being paroxysmal. The intervals between the paroxysms may be entirely free from pain, or may be accompanied by pain of a comparatively dull, aching character. The paroxysms are probably due to the intermittent violent peristalsis of the uninjured portion of bowel above the seat of obstruction. During the progress of the case, the pain may lose this important paroxysmal character, and become more continuous, owing to the supervention of some degree of peritonitis. On the other hand, it will often be noticed that the pain diminishes in intensity or entirely ceases as the fatal event is approached and the sensibility

becomes progressively duller. In cases of somewhat gradual onset, the position to which the pain is referred by the patient may give a clue to the site of the lesion; but in many cases, especially of acute and violent onset, it is felt at the umbilicus, or all across the abdomen at this level, without regard to the position of the obstruction. (2) Tenderness of the abdomen, though nearly always present to some extent, is not a very marked feature unless some peritonitis coexists. In an early stage, at any rate, where there is most need for an accurate diagnosis, it never approaches to the tenderness which is met with in peritonitis. (3) Vomiting is practically always present. It is more frequent and severe in cases of acute and violent nature than in those with a more gradual onset. At first the vomit consists only of the contents of the stomach and then of bile-stained gastric secretion, but sooner or later it becomes stercoraceous, and consists of a thick, dark fluid, with a fæcal odour, which is doubtless derived from regurgitation of the contents of the small bowel into the stomach. This regurgitation is probably due to the violent downward peristalsis occurring in the small bowel, which is more or less full of partly digested food products and its own secretions. By this peristalsis, which acts in a downward direction upon the periphery of the contained column of fluid, the central portion may be conceived to be forced upwards in the reverse direction, until it mingles with the contents of the stomach. Stercoraceous or fæcal vomiting may occur within forty-eight hours of the onset of the illness. It is most apt to appear at an early time when the onset of the obstruction is acute, and when the site of the obstruction is high up in the small intestine. Once established, it continues throughout the illness. (4) Constipation is in nearly all cases absolute from the very commencement of the illness. Although the bowel is of course seldom empty below the point of obstruction, yet, as a general rule, neither fæcal matter nor flatus are passed after the onset of the first symptoms. It may be, however, that in cases of obstruction by carcinoma of the large bowel, a little fæcal matter and gas may be passed naturally or removed by enema from below the stricture, but this only occurs to a very small extent. Such an occurrence in any other form of obstruction (except intussusception, which is separately described) is exceedingly rare, and the rule of constipation is nearly absolute. (5) Distension of the abdomen is nearly always present to some extent. It is most marked in obstruction of the large bowel and in volvulus, and it is absent only when the obstruction is so high up in the small intestine that the greater part of the intestinal tract, small and large, is collapsed. (6) Peristalsis is very often visible through the abdominal wall at an early stage, in cases of obstruction of the small intestine, and at a late stage when the large intestine is involved. It is often accompanied by gurgling or rumbling, of which the patient is aware. The coils of small bowel may often be plainly seen arranged transversely or somewhat obliquely across the abdomen, showing distinct peristaltic waves from time to time, which often correspond to the paroxysms of pain. Or it may be that only slight, gently rounded eminences may be seen at some part of the abdominal surface, which, on careful observation, may be noticed to alter in shape, size, or position, or disappear from time to time. It is generally possible to hear the peristaltic movements with the stethoscope, even when they are not visible. The observation of peristalsis, either by eye or ear, is an important point, as serving to distinguish obstruction from peritonitis. (7) The urine is

generally diminished in amount, and may, especially in acute cases, contain a trace of albumin. The diminution is more marked in acute cases where the small intestine is affected, than in the more chronic forms of obstruction of the large intestine.

In order to obtain a clear picture of the symptoms of obstruction, as produced by the multifarious causes already detailed, a distinction must be made between acute cases, where the onset is sudden and a grave condition is rapidly developed, and chronic cases, where the onset is more gradual and there is more delay before a very grave condition is reached. In both these classes there is the same train of symptoms arising from the interference with the action of the bowels; but in the acute class there are superadded more severe constitutional symptoms, which are due to the damage inflicted upon the bowel at the point of obstruction. A distinction between the acute and the chronic class is a clinical one, and it does not correspond precisely to any pathological classification of the causes of obstruction. But it may be said that to the class of acute cases belong instances of strangulation, of volvulus, of obstruction by a gallstone, some examples of intussusception, and some examples of obstruction by adhesion or compression; while the type of the chronic form is presented by the obstruction produced by a new growth of the large bowel, and sometimes by cases due to adhesions or compression. The symptoms of intussusception differ in some respects from those of the other forms, so that they are best considered apart.

. **An acute case.**—The patient is suddenly seized with severe pain in the abdomen, commonly referred by him to the umbilicus, or roughly, across the belly. He vomits within a very short time, often within a minute or two, though sometimes there is an interval of a few hours, during which the pain may increase in severity. As a rule, the vomiting continues through the whole course of the illness, the vomited matter becoming stercoraceous within a variable period, sometimes within forty-eight hours of the onset, or even less. Occasionally, towards the end, the vomit may contain a little altered blood. The pain is always to some extent paroxysmal. The intervals between the paroxysms are not, as a rule, free from pain, but there is not the continuous unchanging character of the pain of peritonitis. The vomiting, too, is accompanied by retching, which may be extremely distressing, and it differs in this respect from the vomiting associated with peritonitis. Constipation is usually complete from first to last. Neither fæcal matter nor flatus is passed, although the patient may feel a call to stool from time to time.

The abdomen rapidly becomes distended, the more so the lower in the bowel is the obstruction. It may be, on the other hand, that when the obstruction is high up in the ileum, or in the jejunum, that the abdomen, although rigid, is yet flat. There is seldom any great degree of tenderness at first, unless some peritonitis coexists, but there is a considerable feeling of soreness. A very important indication is the detection of distended coils of intestines and of visible peristalsis. In the absence of these signs, gurgling will usually be heard with the stethoscope, which is rarely if ever the case in a general peritonitis. There is sometimes hiccough, the tongue rapidly becomes dry and furred, the mouth is dry, and thirst is distressing. The urine is always scanty, sometimes almost entirely suppressed, and it may become albuminous. The temperature is usually subnormal towards the end; it may be normal or slightly raised in the earlier part of the illness,

but it seldom reaches 101°. The general condition is alarming from the very first. The pulse is much quickened, and becomes progressively feebler through the illness. The face becomes pinched and the eyes sunken. The patient becomes apathetic, his voice is feeble, his hands are cold and damp, and inclined to be blue. Profuse sweats break out on the forehead, and when this point is reached death is at hand. The duration of this class of illness, if unrelieved by surgery, is seldom prolonged beyond one week, and in some cases death may occur as early as the third day. Such is an outline of a case of strangulation of the bowel. It remains to add, that in volvulus of the sigmoid flexure there is commonly an enormous distension of the abdomen, which may be in great part filled by the inflated and twisted portion of the bowel. This form of obstruction, moreover, is often deceptive, especially when the cæcum is affected. On the one hand, vomiting and pain are often inconspicuous features, so that the onset may be less alarming than in other forms. On the other hand, collapse may be more severe, and may set in with surprising suddenness at an early period, and in these cases a large portion of the bowel is often found to be completely strangulated and gangrenous, and death may occur within the first forty-eight hours.

A chronic case.—Obstruction by a growth of the sigmoid flexure may be taken as the type of a chronic case. It is common but by no means constant to elicit a history of increasing constipation, or constipation alternating with diarrhœa, extending back over some weeks or months. Sometimes there is a distinct history of diarrhœa, and a misconception on this point must be guarded against by personal and constant observation of the stools. It will be found that the alleged diarrhœa consists merely of the frequent passage of small quantities of thin fæcal fluid, which has strained through the stricture without giving any real relief to the constipation. And sometimes with this there may be a passage of small quantities of blood. It is sometimes noticed that the motions have been narrowed, but the absence of this appearance is of no diagnostic importance. Sooner or later the constipation becomes absolute, the abdomen becomes distended, and purgatives produce no effect beyond pain or discomfort. Often this point is reached suddenly, the actual cause of obstruction being probably the impaction of a hard fæcal mass in the narrowed bowel, for it may be found post-mortem that a malignant stricture which has proved fatal will still admit the little finger. Even after the actual obstruction has begun there may be a passage of fæcal matter or of flatus, either naturally or in response to an enema, but this comes only from the bowel below the obstruction, and must de discounted. It is more likely to occur, the higher in the large bowel is the seat of obstruction.

There may be impaired resonance in one or both flanks, and, as a rule, the distension of the abdomen is more general than in strangulation of the small bowel, in which case the prominence occurs mainly in front and less at the sides. A tumour may be within reach of the finger by the rectum, but it is seldom to be felt in the abdomen, owing to the distension. The symptoms that have been already detailed as following obstruction of the small bowel, now develop, but with less rapidity. The abdomen becomes more and more distended day by day, vomiting sets in and becomes sooner or later stercoraceous, but pain is seldom severe, and may be entirely absent. The appetite is lost, the tongue becomes thickly furred, and then dry. Peristaltic movements of the small intestine may become visible. The symptoms of collapse set in, and death occurs commonly in the course

of the second week, though it is sometimes much later. In some cases death may be hastened by the onset of peritonitis, due to the rupture of a distension-ulcer in the cæcum.

Intussusception.—The symptoms of an intussusception are more variable than those of other forms of obstruction. The majority of cases are of an acute kind. There is the same sudden onset of pain, which is more or less paroxysmal, and the same vomiting, as in cases of strangulation of the bowel already described. Perhaps it may be said that in the adult both these symptoms are rather less urgent than in cases of strangulation. But in the child the pain is apparently severe. With each paroxysm he cries aloud, writhes, draws up and extends his legs, and may become pale and faint. The vomit consists of the contents of the stomach and later of bile-stained fluid. In adults and older children it may become stercoraceous, but this is not so common as in other forms of obstruction, and in the young children who are more particularly the victims of intussusception it is decidedly rare. The onset may be followed by an action of the bowels, but with this exception the constipation is absolute in the child. There is, however, frequent straining, which is very characteristic of this affection, and from time to time mucus and blood are usually passed. In the adult the constipation may be as absolute as in cases of strangulation, but in some instances there is a passage of a small quantity of liquid fæces from time to time, to which the misleading term "diarrhœa" is commonly applied by the patient's friends. The difficulty which is thus introduced into the diagnosis is usually counterbalanced by the occurrence of tenesmus and the passage of blood, which symptoms occur in about 50 per cent. of cases, and are of great distinctive importance. The abdomen is at first but little distended, and scarcely tender. Between the paroxysms of pain it may even be flaccid. Its condition will thus commonly permit the recognition of the characteristic sausage-shaped tumour which has been already described. This is usually met with in the right half of the abdomen, but it may lie at any point of a semicircular line drawn from the right to the left iliac fossa round the umbilicus. It may be firm and doughy and may have a sharp outline, but any great distension of the abdomen may render it indistinct. The head of the intussusceptum may in children often be felt in the rectum, and it can be distinguished from a tumour or a prolapse by the fact that the finger can be passed completely round it between it and the rectal wall. A tumour can be felt in the abdomen in about 50 per cent. of all cases. The temperature is usually normal, though it may be raised 3° or 4° at a late stage. The course of the illness, and the general condition of the patient are commonly the same as in the case of strangulation. Vomiting continues, the tongue becomes dry, the eyes sink in, the face becomes pinched, and collapse sets in as a rule about the third or fourth day, though life may be prolonged for a week. The rate of mortality varies inversely with the age of the child, and intussusception is exceedingly fatal during the first year of life.

The illness may, however, run a much milder and more chronic course, particularly in adults, and it may then present great difficulty of diagnosis. In such cases the intussusception is small, the lumen remains open, and obstruction is incomplete. The onset may be much less marked and less sudden, so that careful questioning may be necessary to elicit a clear history of it. The salient features of the illness are paroxysmal griping pain in the abdomen, occasional tenesmus, the passage from time to time

of small quantities of fæcal matter and of blood, with occasional vomiting. In this condition the patient may continue for several weeks or even months, with progressive emaciation and increasing feebleness, and so die, unless relieved. Or it may be that after the lapse of some weeks or months an acute obstruction may suddenly arise. Careful examination under an anæsthetic will as a rule reveal the characteristic tumour in some part of the region between the right iliac fossa and the umbilicus.

Diagnosis.—In all cases of intestinal obstruction an attempt must be made to ascertain the cause and position of the disease. Often, however, this is impossible, or the evidence may be only sufficient to warrant a guess.

Anatomical.—In the first place must be considered the question as to whether the obstruction is situated in the small or the large bowel. This point can generally be determined by those differences in the character of the onset and in the early symptoms which are contained in the descriptions already given. It may be generally stated that the higher up in the intestinal tract the lesion is situated, the more violent are the early symptoms, and the quicker is the arrival of the collapse which precedes death. An exception, however, must be made of volvulus of the cæcum or sigmoid flexure. The vomiting follows the initial pain more quickly, and it continues to be more severe, and more quickly becomes stercoraceous. At the same time the urine is more diminished. Additional information can be obtained from the shape of the abdomen, which tends to be more centrally distended in obstruction of the small bowel, and more uniformly distended both as to flanks and centre when the colon is involved. The form of the coils of the small intestine may often be recognised on the anterior abdominal wall, and the pouches of the large intestine may also be distinguished in the same way.

And, further, by palpation and percussion, the emptiness or fulness of the ascending and descending parts of the colon can often be ascertained. The practice of endeavouring to locate the position of the lesion in the large bowel by means of a long tube, or by the injection of fluid, is practically worthless. In cases of carcinoma, situated low down in the large intestine, the motions may have been narrowed before the onset of obstruction; but the absence of this sign is of no diagnostic value.

Pathological.—If the evidence points to the small bowel as the site of the obstruction, the field of possible conditions is very large, and accurate knowledge of all the facts bearing on their causation is necessary for diagnosis. The previous history of the patient must be examined with scrupulous care, bearing in mind the importance of past peritonitis having a pelvic, appendicular, or other origin; of previous hernia, of previous abdominal operation or injury, and of previous symptoms of any kind pointing to abdominal disease. A history of tuberculosis in the patient or his family may be of importance, and previous biliary colic in an elderly patient may be suggestive. A history of gradually increasing constipation, culminating in an acute onset, is sometimes obtained in cases of obstruction by adhesion and by compression, and it may be elicited only by leading questions. The relative frequency of the various forms of obstruction at different ages must be taken into consideration; the frequency of intussusception in children, and of strangulation by Meckel's diverticulum in children and adolescents, being especially borne in mind. Finally, the exact mode of onset may afford some clue. In all cases the hernial apertures within

reach must be carefully examined, but it must be recognised that an incomplete hernia may escape detection.

If the evidence points to the large bowel as the site of the obstruction, the field of possible causes is smaller. The great preponderance of new growth, and its frequency in certain positions, have been already mentioned. A history of previous constipation, perhaps increasing in severity, with some anæmia, emaciation, and failure of general health, may often be obtained, and will point strongly to this condition. It must be remembered also that malignant disease of the intestine may occur at a comparatively early age, and cases have been met with at the age of 20. A history of syphilis or dysentery, or of previous abdominal operation or injury, may also be of importance.

Differential.—(1) Acute peritonitis may present some difficulty. In a general peritonitis there is a more continuous pain. The abdomen is much more tender, there is commonly some rise of temperature, the vomiting is attended with less muscular effort, and the vomited material does not become stercoraceous. Further, there is no movement whatever of the intestinal coils to be detected by the eye or with the stethoscope. In one class of peritonitis, namely, that localised around and originating in the vermiform appendix, there is sometimes a close resemblance to intestinal obstruction, and a mistake is often made. The difficulty arises more especially when the peritonitis is limited to the right lower quadrant of the abdomen, and in consequence of the fixation of the bowels so caused there is a general intestinal distension, and perhaps some peristalsis becomes visible. The diagnosis can be made by noting the difference between the right iliac region and the rest of the abdomen, as regards pain, tenderness, peristalsis, and percussion-note, and perhaps a history of previous inflammation around the appendix may be obtained. (2) Enteritis is, as a rule, associated with diarrhœa, and no difficulty in diagnosis can arise. Rarely, however, in certain severe cases already mentioned, there may be constipation, vomiting, distension of abdomen, and paroxysmal pain. The distinction, which in such cases is difficult, must depend on the difference in the mode of onset, on the fever which is usually present, and on the facts that flatus may be passed, and that the constipation is not absolute from the first, but is commonly preceded by some looseness of the bowels. (3) In chronic constipation, the only confusion can be with a new growth or compression of the large bowel, and a careful investigation of the history must be relied on for the distinction, unless impacted fæcal matter can actually be felt per rectum. (4) Lead colic must always be borne in mind, and the gums examined. Though the pain and vomiting may resemble those of obstruction, and the constipation is usually complete, yet the symptoms, as a whole, are less alarming; there is less quickening of the pulse, and less marked constitutional disturbance. (5) Renal and biliary colic may lead to error on rare occasions. There is the sudden onset of pain, which, in the case of biliary colic at any rate, can sometimes not be accurately localised by the patient, but is referred vaguely to the umbilical region. There is severe vomiting. There is often constipation, and it is sometimes noticed that a biliary colic is accompanied by some degree of flatulent distension of the abdomen. Attention must be directed to such points as previous colic, localisation of the most intense pain about the right costal margin or in the loins, the presence of an icteric tint of the conjunctivæ, the continuous character of the pain, and the absence of signs of increased intestinal peristalsis. (6) The rare con-

dition known as acute hæmorrhagic pancreatitis may be indistinguishable from an intestinal obstruction. If the abdomen should be explored in this condition, it is important that the operator should be familiar with the appearance presented by a fat-necrosis, which is commonly present.

Prognosis.—Any form of intestinal obstruction is a grave condition, and in nearly all cases the natural tendency is towards speedy death. But, owing to the steady advance in surgery, the prognosis becomes more favourable year by year. The acute forms of obstruction, which are usually associated with severe damage to the bowel wall, prove uniformly fatal if left unrelieved, and the recovery of the patient will depend mainly on the earliness of operation and the technical skill of the operator. Cases of recovery are now common. In the more chronic forms, especially those produced by growth in the large bowel, there is less immediate danger to life. But though relief to the obstruction is readily given by operation, in some cases the growth cannot be removed, and it must be left to run its course unchecked.

Treatment.—The feeding of a patient suffering from acute intestinal obstruction is a matter of the first importance. It is certainly useless and probably harmful to attempt to give any nourishment by the mouth. When the mouth is very dry and there is great complaint of thirst, small quantities of iced barley-water may be allowed, but even this should be used as sparingly as possible. The patient's strength must be maintained by such food as can be assimilated from the rectum. Nutrient enemata (4 oz. for an adult), each containing milk, strong beef-tea, the white of an egg, and a teaspoonful of liquor pancreaticus, must be given at least every four hours; and if there is any irritability of the rectum or sign of the return of the enema, a nutrient suppository may be given alternately with the enema every three or four hours. The replacement of one enema in the twenty-four hours by half a pint or more of warm water, containing an ounce of brandy, is of use in relieving thirst. In the next place, something must be done to allay the pain. Hot fomentations, with or without belladonna, are certainly of some use; but in all cases, except where operative measures can be undertaken at once, some morphine is necessary. In quarter-grain doses subcutaneously its effect is very striking. The pain is to a great extent relieved, the peristalsis is less violent, the pulse becomes slower, the feelings and looks of the patient undergo improvement. It must be remembered, however, that this apparent improvement is fallacious and temporary, and that it may obscure the gravity of the case. The use of morphine may undoubtedly postpone death, but it can do no more. Washing out of the stomach is often found to contribute to the patient's comfort, acting, as it seems to do, by allaying the distressing peristalsis. As regards more active measures, it should be made a routine practice to administer skilfully a large enema. No harm can result, no time is lost, and it is possible that a mistake in diagnosis may thereby be obviated. After a fair trial there is no object in its repetition.

It may be said that in all cases of acute obstruction, abdominal exploration, as soon as may be, affords the only chance. The mortality, even with the help of surgery, is still very large; but a great part of this mortality is due to delay, for which an over free use of opium is often responsible. The great advance in abdominal surgery renders it possible to cope successfully with nearly every kind of intestinal obstruction, and examples of the cure

of cases which have up to this time inevitably proved fatal are now abundant. Bands may be found and divided, even old and complicated adhesions have been separated, a volvulus has been untwisted, and insuperable obstruction due to adhesions has been circumvented by the establishment of intestinal anastomosis. In some cases of old and complicated adhesions and matting of intestines, such as is sometimes met with as the result of peritonitis around the appendix, and more commonly as a result of tuberculous peritonitis, restoration of the freedom of the bowel may be impossible. In some such cases there is a possibility of making an anastomosis between suitable portions of the bowels. In some instances, however, surgery is powerless. In such cases the puncture of the bowels through the abdominal wall with a fine trocar is perfectly safe, and may be frequently repeated; but such short lengths of bowel only can be emptied of gas in this way, that the relief is of short duration, and often trifling in amount.

All that has been said as to the management of a case of acute obstruction holds good in the chronic forms, though nutriment may sometimes be administered by mouth. There is, however, more time allowed. A trial of copious enemata preceded by an injection of 4 oz. of olive oil, administered by a long tube, may be made and repeated. And if there is any chance that the cause of the obstruction is a fæcal impaction, there is no harm in giving castor-oil by the mouth. If it fails, the patient's condition is in no way aggravated. The majority of cases can here again be dealt with successfully by surgery, and by surgery alone. The details belong to the surgeon's province, but colotomy will in nearly all cases afford relief. In many cases of carcinoma of the sigmoid flexure, which is by far the most common cause of this form of obstruction, the growth can at the time, or subsequently, be entirely removed, and the integrity of the bowel may be restored. In the case of growth about the cæcum and ascending colon, the establishment of anastomosis between the small bowel and some part of the colon below the obstruction affords a reasonable hope of success.

As regards the treatment of intussusception, some special points are to be noted. The general management of the patient as regards diet, opium, and local applications is the same as in other forms of intestinal obstruction; but the condition is one which will clearly be aggravated by a purgative or an enema. In the case of an acute intussusception, an attempt should always be made at reduction, and in a great many instances this can be successfully effected. It should be undertaken by a surgeon who is prepared to operate at once if it fails. Air pressure may be employed by means of simple bellows, or by means of Lund's inflator; but the use of fluid is much safer, more easily regulated, and more effectual. The child should be placed under the influence of chloroform, the buttocks raised by a pillow, a tube introduced into the rectum, packed round with tow, and salt-solution at 100° F. may thus be introduced under steady control by means of a soft indiarubber tube, and a funnel. The force is obtained by raising the funnel, and a height of 3 ft. above the anus may be safely employed, while the course of events is followed as far as possible by one hand upon the tumour in the abdomen, and the general condition of the child is carefully watched. In many cases, reduction can be effected in this way, and this method has been successful even after the lapse of four or five days. After reduction, great care must be exercised in the next few days to prevent a return. The movement of the

intestine must be kept in check by the free use of opium, and feeding must be by the rectum only.

In many cases, however, even of recent standing, this method will be found to have failed to completely reduce the intussusception, the last part of the intussusception being always the most difficult part to return. When this is found to be the case, or when the intussusception has been of some standing and adhesions have already formed, immediate surgical operation affords the best chance of relief, and should in all cases be employed without any delay. Even in young infants many successful results have been recorded.

CONSTIPATION

A natural variation is met with in different individuals as regards the action of the bowels. In the majority there is a call to stool once a day. Some, however, have an action of the bowels only every other day, others habitually twice a day. In some individuals symptoms arise if a day or two has passed without action, whilst others neither feel nor show any ill effects after a week's absolute constipation. By constipation, therefore, is meant a retention of fæces which is unnatural in the individual.

Etiology.—The causation is an exceedingly complex subject, bringing into review all parts of the body. A natural healthy action of the bowels depends on a variety of factors. The formation of fæcal matter in a proper plastic condition for evacuation is mainly a function of the large bowel. Here water is taken up from the food waste, and the proper consistence is attained. But it is necessary also that the whole process of digestion in the stomach and small intestines should be efficiently performed, and that the secretions of these parts and of the liver and pancreas, should be normal in quantity and quality. Dyspepsia of various kinds is often attended by constipation. Further, it appears that the food residue entering the large intestine should have a certain minimal bulk which allows of its passage onwards by peristaltic action. If it falls below this bulk, there is a tendency to delay in its passage down the large intestine, to continued loss of water, and consequent hardening of the fæces. The diet is therefore an important matter. This hardening results whenever there is not a daily, or at all events a regular evacuation, and every day of constipation adds to the difficulty. Thus may arise habitual constipation in servants, school-boys, and busy men, who are for different causes pressed for time in the morning.

It is clear that for the due performance of the function, the nervous and muscular mechanism of the bowel must be in perfect order. Both these are probably impaired by the over-distension of the bowel, which ensues from constipation of any origin, and the evil is thereby aggravated. For the perfection of both mechanisms it is necessary that the body as a whole should be in perfect health. Anæmia, neurasthenia, fever, and ill-health from any cause, are commonly accompanied by constipation. It is troublesome also in paraplegia and many cases of chronic brain disease. Exercise is essential, partly by its general effect on the body, partly perhaps by some mechanical stimulation of the abdominal muscles, and perhaps of the bowel. Sedentary habits are a fertile cause of persistent constipation, and thus women are particularly prone to be affected. The troublesome constipation of diabetes is probably to be attributed to

the loss of water associated with that condition. Unusual exercise with profuse perspiration is often followed by constipation. A change of locality, diet, or habits will often induce some irregularity in a previously well-regulated individual. Finally, a fissure of the anus or some pelvic condition in women, which makes defæcation painful or difficult, must always be borne in mind. In many cases of chronic constipation, it is extremely probable that the difficulty is partly the result of a long, large, and dependent sigmoid flexure. It is possible that this is a congenital condition, but in some cases it is probably the outcome of habitual neglect of the bowels during early life.

Morbid anatomy.—The primary changes in the bowel which lead to constipation have been already mentioned in connection with the subject of obstruction. It may be added that in some cases constipation probably arises from some congenital abnormality in the length and arrangement of the sigmoid flexure, though no actual facts can be quoted. Important secondary changes in the bowel may be produced by constipation, but it must be remembered that these are exceedingly rare when the great frequency of constipation is considered. The sigmoid flexure may become much dilated, and may come to fill the pelvis and to exercise pressure on veins and nerves on both sides of the body. Hypertrophy of the muscular coat of the descending colon may be met with, such as has been described in connection with carcinoma of the sigmoid flexure. Enormous dilatation of the whole colon may occur. In a specimen in St Thomas's Hospital Museum, taken from a man, æt. 28, who had suffered from habitual constipation, the large intestine measures 6 in. in diameter for the great part of its length, and the descending colon is 2 in. wider. More than fifteen quarts of moderately firm fæces were removed from the large intestine after death. Ulceration of the bowel is sometimes seen, more particularly in the cæcum. The ulcers are sometimes due to distension of the bowel, but sometimes they are probably produced by the mechanical irritation of hard scybala.

Symptoms.—The effect of chronic constipation upon the patient is often surprisingly slight. In many cases an individual may with difficulty procure an evacuation by one means or another every three or four days, and yet he may be conscious of no impairment of health. It is not uncommon to see chlorotic girls, who have had no action for a week or ten days, and yet have no special symptoms. The chlorosis of young girls has indeed been attributed to constipation, but though constipation is certainly very general in such cases, it is not invariably present, and, on the other hand, it may exist for many years without production of any anæmia.

Some individuals are subject to headache when constipated. They lose something of their appetite, and the tongue becomes furred. They may become irritable or depressed, complain of loss of energy, and are disinclined to exertion. In some cases the mental condition is more serious, especially in neurasthenic individuals. They become seriously depressed, their thoughts are more and more concentrated upon the state of the bowels, until the brooding upon this subject may lead them over the border line into hypochondriasis.

Sometimes by pressure upon lumbar or sacral nerves, pain is produced down the front or back of the thigh. Though this is more common on the left side, it may also occur on the right. By pressure on intrapelvic veins, hæmorrhoids or varicocele may be developed or

aggravated, and even œdema of one or both feet may occasionally result. On examination of the abdomen, fæcal masses, which can be indented by pressure, if the abdominal parietes are thin, may be felt in various positions, in the cæcal region, under the liver, or anywhere in the course of the colon. Such masses in the cæcum must not be confounded with the inflammatory hardening of perityphlitis. They are most common in the sigmoid flexure, where a large roll may often be found. In some cases the rectum is found to be completely filled by hard scybalous masses, so that the introduction of a finger past the anus is hardly possible. This may even be the case, especially in women, when no complaint of constipation has been volunteered by the patient. In such cases care must be taken not to be deceived by a history of diarrhœa. Small quantities of fæcal fluid may drain away at frequent intervals, even when the rectum and sigmoid flexure are almost entirely filled with impacted scybala. On rare occasions it has been noticed that an attack of constipation in a previously healthy individual may be attended by a moderate degree of fever, the temperature reaching 100° or 101° for a day or two, but such cases should be carefully examined for evidence of disease of the appendix.

Long-standing constipation may terminate in a veritable obstruction by impacted fæces, but this is a very uncommon event, considering the great frequency of constipation. It is more common in females than in males. The onset of the more severe symptoms is usually gradual. The constipation becomes less and less amenable to treatment. No doubt a considerable length of the colon is in such cases distended by fæces to such a degree that any feeble contractile power that may remain is unable to dislodge the impacted mass. The abdomen becomes distended, peristalsis is visible, nausea and vomiting begin, the vomit acquires a stercoraceous odour, and the whole appearance and general condition are identical with those of a patient suffering from obstruction due to carcinoma of the sigmoid flexure. A differential diagnosis can hardly be made save by means of the previous history. In rare cases the actual onset of acute symptoms is sudden. It is then due to the sudden blocking by a hard fæcal mass of an already partially obstructed bowel.

Treatment.—In all cases care must be taken, in the first place, to find any specific cause among those above enumerated to which the constipation can be attributed, and to correct it so far as possible by appropriate treatment. The patient must be impressed with the necessity of yielding to any call of nature without delay, and in the absence of any such call to make a daily attempt at a regular hour, preferably after breakfast. Some alteration in the daily habits may be necessary for the deliberate fulfilment of this matutinal function. In many cases, especially in large towns, the remedy will lie in the enjoinment of regular exercise, on horseback, on a bicycle, or on foot. The diet must be rigidly examined, and though it may be apparently healthy, an addition of further green vegetables, of fruit according to season, of brown bread, and of porridge, is often beneficial. Excess of meat, eggs, and milk in the diet must be guarded against, and a tumblerful of water during dressing before breakfast should always be tried.

In some cases which are in an early stage, nothing further is necessary; or an aloes pill, cascara sagrada, calomel, a seidlitz powder, or some mineral water, may occasionally be required. But the constipation has usually become a confirmed habit before the patient comes under observation,

and drugs must be employed with care. There is no doubt that the majority of the purgatives which may legitimately and usefully be employed for occasional attacks of constipation do actual harm when it has become habitual. The principle of treatment is to overcome the habit patiently and slowly, rather than to purge. In the common type of case, aloin is the safest drug. It must be used tentatively, so as to find the exact dose which, given overnight, produces a fair action in the morning. Commonly a pill containing 2 gr. of aloin, half a grain of extract of belladonna, and a quarter of a grain of extract of nux vomica will in an adult have this effect. An addition of half a grain of ipecac. powder is sometimes made with advantage. It is wise to use too little aloin rather than too much. With the required pill an attempt must be made to get a daily action, by giving it for a time every night. When a daily action has been thus established, the use of the drug must be gradually discontinued. At first the dose of aloin should be diminished; later the pill should be used only on alternate nights, and if necessary an occasional glycerin suppository in the morning, or a lozenge containing 5 gr. of precipitated sulphur and 1 gr. of acid tartrate of potash in the evening may be substituted. If the habits and diet are at the same time skilfully regulated, the patient may be often brought back to a healthy condition. Sometimes, in slighter cases, 3 or 4 oz. of Hunyadi Janos, or Friedrichshall, or Rubinat water, with an equal amount of hot water, may be used in the morning before breakfast, with the same intention of intermitting and discontinuing its use as soon as may be. Or an artificial Carlsbad salt may be used in the same way, containing 30 gr. of sulphate of soda, 15 of bicarbonate of soda, and 5 gr. of chloride of soda in a tumbler of hot water. In more severe cases it may be necessary to give aloin three times a day at first, always stopping short of free purgation.

Chronic cases are, however, often met with, where all these means fail. The large bowel has seemingly lost much of its muscular power, and possibly the sigmoid flexure is large and dependent. Even here violent purgatives must be considered only as a last resource. The rectum must be examined, and if hardened fæces are found to fill it, there is no other course to be pursued than their mechanical removal. Recourse must then be had to soap-and-water enemata, by the daily use of which and the occasional use of castor-oil, the large bowel must be kept as empty as possible, with the hope that it may recover something of its power. At the same time, electrical treatment and abdominal massage may be employed with advantage. Such cases may, under this treatment, get back to a comparatively comfortable condition, so that with correct diet, habits, and exercise, and with an occasional dose of castor-oil or aloin pill, a fairly regular action of the bowels may be obtained. But in some cases it must be realised that the improvement is very slight, and enemata and aperients of all kinds may be required to the end of the chapter. It has happened in cases of complete atony of the large bowel, with impaction of fæces and definite signs of obstruction, that colotomy has been necessary, but such a necessity is of very rare occurrence, and need not be anticipated.

APPENDICITIS.

Inflammation of the vermiform appendix is a common occurrence, and it is important, owing to the frequency with which peritonitis is excited. The peritonitis may be either general, or localised in the neighbourhood of the appendix. In the latter case it may be limited to the exudation of a coagulable inflammatory material, which can undergo absorption and removal (simple perityphlitis), or result in the formation of pus (perityphlitic abscess). In clinical usage the term appendicitis is often loosely extended to denote any peritonitis which arises around and in consequence of a diseased appendix.

Etiology.—It is probable that appendicitis can only be recognised clinically when the inflammation has involved its peritoneal coat, or the peritoneum in its neighbourhood; and it is therefore not possible to distinguish accurately between the causes which lead to the primary disease of the appendix and those which lead to the secondary production of peritonitis around it. It is reasonable, however, to suppose that the proneness of the appendix to inflammatory and microbic disease, as compared with the cæcum and the rest of the intestinal tract, is mainly due to its obsolete and functionless condition. And it is possible that slight causes of inflammation, such as cold, and the presence of indigestible material, which pass unnoticed in other parts of the intestine, may provoke disease in this rudimentary organ. There is evidence also to suggest that a severe form of appendicitis may be attributed to a rise in the virulence and pathogenic power of some of the micro-organisms which normally inhabit the part, particularly *B. coli communis*.

Appendicitis, including under the term all the resulting forms of peritonitis, is most common in the young. More than 50 per cent. of the cases occur under the age of 20, and only 15 per cent. occur after the age of 30. It may, however, be met with at both the extremes of life. It is much more common in males than females, in the proportion of 7 to 3. It occurs in all occupations, and in all classes of society. The onset of an attack may occur without warning or apparent cause in a healthy individual. In some cases there is a history of previous constipation. Sometimes it is immediately preceded by an indigestible meal, or by an injury or strain; but these factors are probably of importance only in setting up peritonitis around a previously diseased appendix.

Morbid anatomy.—The diseases of the appendix which are apt to excite some degree of peritonitis are—(1) a catarrhal inflammation, which is more or less strictly limited to the mucosa; (2) an ulceration, which is usually due to the pressure of a fæcal concretion or a foreign body; (3) an infective inflammation, which involves all the tissues of the appendix wall, and is always associated with, and probably due to, an invasion of the wall by the bacteria which inhabit the bowel.

A tuberculous ulcer in the appendix may set up a perityphlitis; but it is an uncommon cause of this condition. A typhoid ulcer in it may perforate and excite a general peritonitis. Actinomycosis has been known as the cause of a perityphlitic abscess.

Catarrhal appendicitis.—This form is frequent, and it is probable that it often occurs without symptoms. The changes are those of inflammation of mucous membranes elsewhere. The epithelium of the general surface and of the crypts of Lieberkühn is shed. The retiform tissue which forms the groundwork of the mucosa becomes infiltrated with

leucocytes, and it is consequently swollen. The lumen, as a rule, contains no fæcal matter, but it may be occupied by a mass composed of leucocytes, granular débris, mucus, and epithelium. The latter, when derived from the crypts, sometimes appears in the form of definite casts. In a later stage the basement membrane may be destroyed, the infiltration becomes more marked, and the interior of the appendix may come to be lined, in whole or in part, with a layer of raw granulation tissue.

Recovery, doubtless, readily occurs in an early stage by a growth of new epithelium from the remains of the original lining. In some cases, however, where the denudation and destruction of the basement membrane have been complete over a large area, further changes occur in one of two directions. On the one hand, the condition may become one of chronic catarrhal appendicitis, which is a constant source of trouble. While the inner surface continues as a pus-forming granulation tissue, the muscular coats may be infiltrated with leucocytes and connective tissue cells, and there is great increase in their fibrous elements, so that the whole wall of the appendix becomes thick, rigid, and incollapsible. On the other hand, union may occur between the apposed granulating surfaces, so that the lumen of the tube may be in part, or in its whole length, obliterated by the formation of fibrous tissue. If obliteration takes place in the whole length of the tube, the appendix ceases to be a source of disease. It not uncommonly happens, however, that obliteration occurs only at some one point, and a stricture thus results, which is usually situated near the cæcal end of the organ. The peripheral part of the appendix may subsequently become distended into a cyst by its own secretion of pus, or muco-pus, which can find no outlet, and the cyst so formed may be 2 in. in length by 1 in. in breadth. Owing to the continuance of inflammation in the cystic portion, aided by the tension of its wall, rupture or perforation is not an uncommon event. It should be mentioned that a similar cyst may be developed through the kinking of the tube at its cæcal end, and in such a case the contained secretion will escape when the organ is made straight.

Ulcerative appendicitis.—Ulceration of the appendix may occur in a late stage of catarrhal inflammation, especially when a cystic condition has been reached. But the ulceration which is more particularly included under this head results from the pressure of a fæcal concretion or a foreign body. A concretion has been variously estimated as being the cause, in from 30 to 50 per cent. of all cases of appendicular peritonitis. It is formed by the lodgment in the tube of a pellet of fæcal matter, which becomes moulded by the peristaltic contractions into an oat-shaped or oval body, often resembling a cherry-stone. This loses its water, and its hardness is further increased by the deposition of lime salts upon it. In some cases a foreign body, such as a splinter of wood or a pin, has been found as the nucleus of a concretion. Two or more such concretions, in various stages of hardness, may be found in the same appendix. A foreign body is much less common, and the frequency of its occurrence has been variously estimated as from 4 to 12 per cent. All kinds of small bodies which are apt to be inadvertently swallowed are found, such as fruit stones, pips, seeds, pieces of bone, nutshells, shot, nails, pins, bristles, and leaves. Each such concretion or foreign body is apt, by its pressure, to produce a progressive ulceration at the site of its impaction, and the process continues until the peritoneum becomes involved, or actual perforation of the appendix wall occurs.

Infective appendicitis. — This form of inflammation is extremely fatal, and it is the cause of at least 50 per cent. of fatal cases of general appendicular peritonitis. It may arise suddenly in an appendix which is cystic, or in one which is already the seat of ulceration, or in the case of a chronic catarrh. In all these conditions the protective epithelium has been more or less destroyed. It may arise also in an appendix which shows little or no evidence of any previous disease. In all cases of infective appendicitis the submucous and muscular coats are found, both during life and after death, to contain numerous bacteria, for the most part *B. coli communis*, and it is probable that the changes are closely connected with this invasion.

The changes included under this head vary greatly in severity and extent. Most commonly there occurs a necrosis or sloughing of some part of the wall of the tube in its whole thickness. Sometimes an inch or more of the appendix may undergo necrosis in a large part of its circumference. Sometimes the process occurs in the whole circumference, so that the tip may die *en masse*, or the organ may be more or less completely divided into two parts, and sometimes the whole organ may be detached in this way from the cæcum. In other cases the necrosis may be more limited in degree, and it may be indicated upon the outside of the tube only by a discoloured area, in which may be situated one or more minute apertures, which penetrate the peritoneal coat, but do not necessarily lead into the lumen. In rare cases, again, there may be no actual necrosis, but there may be observed, microscopically, the signs of acute inflammation of the submucous and muscular coats, including, perhaps, the formation of minute abscesses in the substance of the wall.

Finally, it must be mentioned that the length and situation of the appendix are variable, and some unusual clinical features in the peritonitis, resulting from its disease, are thereby explained. The average length in the male is 3½ in.; in the female, 3 in. The extremes are about 1 in. and 9 in. Most commonly (about 44 per cent.) it runs upwards along the left border of the cæcum, or upwards and inwards, or directly inwards across the psoas. It often (about 26 per cent.) lies behind the cæcum, and its tip may even rest on the right kidney. Often, also (about 17 per cent.), it hangs down into the pelvis. In some cases it is curled up on the tip of the cæcum, or in the ileo-cæcal fossa; and sometimes it runs up on the outer side of the cæcum. It has been found in the sac of a hernia. Its tip has often been found lying to the left of the middle line, and it may even reach the left psoas. Its variability in position is increased also by the fact that the cæcum is sometimes found to be placed higher than usual, and to have no relation to the iliac fossa.

Any one of the morbid conditions of the appendix above described is apt to be attended by an inflammation of some part of the peritoneum.

(*a*) In the mildest and commonest form (simple perityphlitis), only that part of the peritoneum is affected which covers the appendix, the cæcum, and the coils of small intestine which happen to be situated in the right iliac fossa. The inflammatory exudation which appears on the peritoneal surface, and which tends to accumulate in the interstices between the intestines, undergoes coagulation, and the parts lying in the right iliac fossa are thereby fixed, and form a firm, coherent mass, which may usually be readily felt with the hand. Recovery from such an attack is almost invariable; the exudation is mainly absorbed, but is partly in some cases replaced by

organised adhesions. A recurrence is apt to take place. This simple perityphlitis, which accounts for 70 per cent. of all cases of peritonitis arising from disease of the appendix, is most commonly associated with a simple chronic catarrh of that organ, but may arise from the cystic condition, and from the presence of a concretion without perforation.

(*b*) In a small number of cases (about 15 per cent. of all forms of appendicular peritonitis), the inflammation, while still remaining limited to the parts situated in the right iliac fossa, assumes a pyogenic character, presumably owing to the escape of bacteria from the diseased appendix. Pus then accumulates around the appendix (perityphlitic abscess), forming for itself a definite cavity, which is usually walled in and shut off securely from the general peritoneal cavity by adherent intestines. Variations in the position of the abscess will be mentioned later. Such a perityphlitic abscess is commonly associated with an ulcerative appendicitis, due to a fæcal concretion, or to a chronic catarrh upon which an infective appendicitis has supervened. An abscess may develop without any visible perforation. *B. coli communis* is in nearly all cases present in the pus; sometimes associated with *Streptococcus pyogenes*, and perhaps other pyogenic microbes.

(*c*) In the third class, about 15 per cent. of all forms of appendicular peritonitis, the whole or the greater part of the peritoneum is inflamed (general peritonitis). The inflammation may be attended with a coagulable exudation, and in such cases recovery is possible; but, as a rule, the whole peritoneal cavity becomes infected with the bacteria above mentioned, the exudation is purulent, the toxic products of the bacterial life are absorbed into the circulation, and recovery is a rare event. A general peritonitis is associated with an infective appendicitis, and with perforation in the course of ulceration, due either to a fæcal concretion or to the cystic condition.

Symptoms.—**Simple perityphlitis.**—In most cases the onset occurs suddenly, without any discoverable exciting cause. Sometimes, however, it is preceded by an indigestible meal, a strain, or a direct injury to the abdomen. The first symptom is almost invariably pain in the abdomen, which is slight or severe. It may be so sharp as to simulate a renal or biliary colic. The pain may be referred from the first to the right iliac fossa, but as often as not it is at first felt all across the abdomen at the umbilical level, and only shifts to the region of the appendix after the lapse of twenty-four or thirty-six hours. Occasionally, at a later stage, some pain attends the act of micturition, owing to the implication of some part of the peritoneal surface of the bladder. And there may also be some pain down the front of the right thigh.

The patient usually vomits within a few minutes or hours after the onset of the pain. The vomiting may continue at intervals for a day or two, especially if the patient is not under treatment; but it is seldom an urgent symptom. With the pain and vomiting are sometimes headache, a feeling of chilliness, and general malaise. The tongue becomes furred, and the appetite is lost. The face may be flushed or pale, and expressive of pain. As a rule, the bowels are constipated from first to last. Occasionally the first onset of the pain is accompanied by one or two loose stools, and in rare instances the bowels are loose throughout the illness. The urine is scanty and high-coloured, and often contains indican.

Tenderness in the right iliac fossa is constant, and in an early stage it may be the only clue to a diagnosis. It is often very acute, and the skin is hyperæsthetic. The extent of the tenderness varies with

the amount of peritoneal surface inflamed, but the greater part of the right half of the abdomen may be tender even in a case which is going to run a simple and favourable course. However widespread, the tenderness is always most marked in the immediate neighbourhood of the appendix, and its maximum point (M'Burney's point) is usually to be found at a spot one-third of the way along a line drawn from the right anterior superior spine to the umbilicus. This point is sufficiently constant to be of diagnostic use, and pain or discomfort may usually be elicited by deep pressure at this spot, even after the subsidence of a perityphlitis, if the appendix remains diseased.

During the first day or two of the illness, the abdomen is commonly slightly distended, and the muscles are somewhat rigid over its right side. As a rule, the muscular rigidity soon passes off, and something of the nature of a tumour can nearly always be felt in the right iliac fossa. This may be soft and ill-defined, but it is usually fairly hard, and its upper and inner borders are sharp. It is commonly oval in shape. It lies, as a rule, above the outer half of Poupart's ligament, but occasionally it is situated nearer to the middle line of the body, so that it comes within reach of a finger introduced into the rectum. It must be noted, however, that difficulty in diagnosis may arise in certain rare cases, when the appendix is situated in some unusual position. If it is placed partly within the pelvis, there may be tenderness, but no tangible mass in the iliac fossa. If it lies under the cæcum, or upon its outer side, tenderness and resistance will be situated above the anterior superior spine, or even in the flank. In all other respects, such cases run the usual course. The iliac swelling may be no larger than a hen's egg, or it may measure 4 in. in transverse and vertical lines. This inflammatory mass, which is very characteristic of perityphlitis, is usually composed of omentum, a loop or two of small intestine, and the cæcum. These structures are found to be congested and œdematous, and the interstices between them contain a variable amount of coagulated fibrinous exudation, which fixes them in the iliac fossa around the diseased appendix. The size and hardness of the mass are sometimes increased by fæcal matter which is retained in the affected portion of the bowel. Resonance is generally impaired over the mass; but sometimes the note obtained by gentle percussion is unaltered, or even tympanitic, if a coil of gas-containing bowel happens to lie on the surface. Owing to this fixation of a portion of the small bowel in the iliac fossa, increased peristalsis occurs occasionally elsewhere in the abdomen. Rumbling and gurgling may sometimes be heard and felt, and peristaltic movements may even become visible. The conjunction of such a symptom with abdominal pain, vomiting, and constipation may arouse some suspicion of intestinal obstruction, but instances are rare where the diagnosis presents much difficulty.

The temperature rises rapidly at the onset of the illness, and commonly reaches 102° or 104° in the first twenty-four hours (Fig. 91). A higher temperature is occasionally met with, but it need cause no anxiety. The maximum is reached during the first three days, often on the first day, and, as a rule, there is a steady fall from this point, the common duration of the fever being from six to ten days. Sometimes, about the beginning of the second week, the fever ends as suddenly as in pneumonia (Fig. 92). Rarely, in a simple perityphlitis, without the formation of pus, a secondary rise of temperature may set in during the course of the illness (Fig. 93). Occasionally the febrile period is prolonged, and it may

extend over three or four weeks, with perhaps a day or two of normal temperature now and then.

About the end of the first week the fever subsides, the tongue becomes cleaner, and the appetite begins to return. Perhaps the bowels may act naturally. The inflammatory induration in the groin shows a progressive diminution in size, and it is less and less tender. As a general rule, all acute symptoms are at an end in ten to fourteen days, but occasionally a little tenderness may persist, with slight fever and a furred tongue for a week or two longer. Recovery from a simple perityphlitis, without suppuration or other complication, is almost invariable, though a recurrence of the attack is exceedingly common. It is more serious, however, in women, for it is apt to produce a miscarriage. After the subsidence of an attack, a swollen, thickened, or cystic appendix may sometimes be felt. Sometimes also there may be present for some weeks a roll of thickened adherent omentum which may closely simulate the appendix in size and shape.
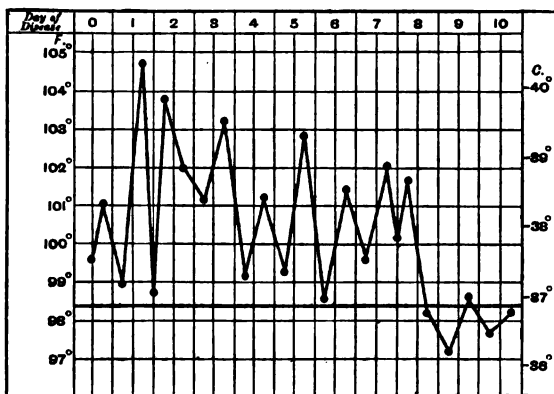
Fig. 91.

The tendency to recurrence is so strong, that a certain class of case is often termed relapsing perityphlitis. A recurrence has been variously
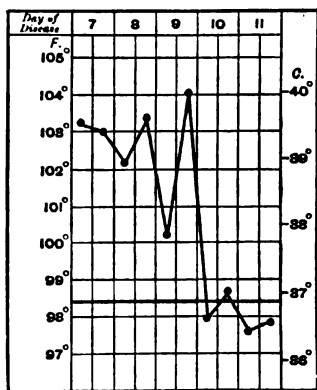
Fig. 92.
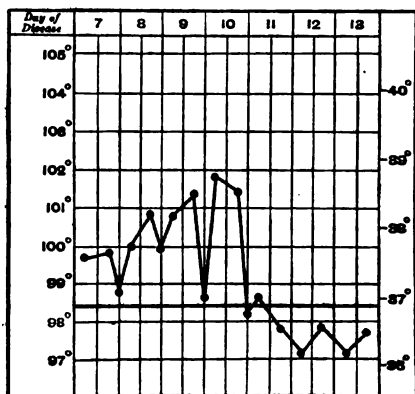
Fig. 93.

estimated as occurring in from 23 to 44 per cent. In some instances, by no means uncommon, one attack succeeds another, with very short intervals of health. Fifty attacks have been said to occur in eight years, and twelve attacks in one year. The individual attacks do not differ from the simple perityphlitis already described, but, as a rule, they tend to become less severe as time goes on. On the other hand, it must be remembered that any one of them may end in suppuration, or may take

the form of a general peritonitis, which is very commonly fatal. The states of the appendix which are most commonly associated with the relapsing perityphlitis are a cystic condition and a chronic catarrh. Less commonly a concretion is found to be present.

Perityphlitic abscess.—As in the case of simple perityphlitis, so in the case where an abscess is formed, the onset of symptoms is in a small proportion of instances immediately preceded by a history of an indigestible meal, a direct injury, or a strain. The early symptoms, moreover, in the two conditions of simple and suppurative perityphlitis are identical, and during the first few days it is impossible to foresee whether the illness will run the simple course, or whether an abscess will arise around the appendix. So that in all cases presenting the symptoms which have been detailed, as indicating local peritonitis in the right iliac fossa, the attention must be directed to the possibility of the formation of an abscess in this position, and to its early recognition.

If the patient is seen for the first time at the end of the first week, or later, it may be impossible to determine at one interview whether pus is present or not, because its recognition rests not so much on any
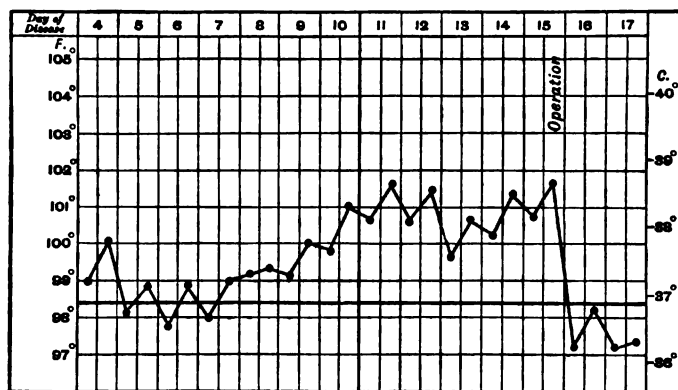
Fig. 94.

specific physical signs or symptoms as on a careful observation of the whole course of the illness. The signs by which the presence of an abscess is recognised elsewhere are commonly absent in the case of a perityphlitic abscess. There is usually no redness of the skin and no œdema, except in cases of long standing, and fluctuation cannot be detected save sometimes under an anæsthetic. Similarly, rigors are seldom if ever met with. The diagnosis of abscess formation must depend on the daily observation of the inflammatory mass in the groin, of the temperature, and of the general condition.

As regards the first point, evidence of pus is afforded either by the maintenance of the inflammatory mass unaltered for an unusual period of time, or by the occurrence of a further increase in its size after the first few days of the illness, or a further increase in its tenderness. The larger and the harder is the tumour, the more likely is it to contain pus. As a rule, in simple perityphlitis, the mass, having attained the maximum size in the first week, remains stationary for a day or two, losing its tenderness, and then begins to subside. As regards the second point, an important indication of suppuration is an unusual continuance of

high fever, or a secondary rise of temperature after a fall has set in (Fig. 94). It must be remembered, however, that both these events may sometimes occur in a simple, non-suppurative case. Finally, evidence must be obtained from the condition of the tongue, from the appetite, from the frequency of the pulse, and from the appearance and feelings of the patient.

By a consideration of all these points taken together, the presence of an abscess can usually be recognised at an early period, in cases that have been watched throughout their whole course. At the same time, it must be remembered that the danger of rupture into the general peritoneal cavity of an abscess, which remains unopened, is extremely slight if the patient is under careful treatment in bed. And under these conditions, a delay of a day or two in opening the abscess is of no great importance, as the protective intestinal adhesions which surround it are of considerable strength. The most certain indications of an abscess in the course of the second week of the illness are given by the continuance of a large, hard, tender mass, the absence of a fall in the temperature, or the presence of a secondary rise, the continuance of a quick pulse, and of a furred tongue.

The abscess varies much in size, but it commonly contains from 2 to 4 oz. of pus. The inflammatory mass in the groin is often the size of a man's fist, but it may be much larger. It may extend upwards nearly to the right costal margin, or inwards across the middle line. Its cavity has usually the abdominal wall for a roof, and the cæcum and iliacus or psoas for a floor, with a wall of adherent bowel on the left. If it is small, however, there may be small intestine between it and the abdominal wall, and the pus is deeply placed alongside of the cæcum. The cavity often has one or more processes which run in various directions, especially into the pelvis among the adherent intestinal coils. If the appendix dips into the pelvis, a resulting abscess may lie entirely below the brim of the pelvis. In such a case it may happen that it can be felt only on examination by rectum or vagina, and diagnosis may be very difficult. In women it often cannot be distinguished from the result of disease of the uterine appendages. It is possible also that in the case of a retrocæcal appendix an abscess may be developed in the flank, or even high up under the right costal margin. A subphrenic abscess may be found, and there is then some risk that the diaphragm may be perforated, and a suppurative pleurisy developed. Cases have also occurred where, owing to the freedom and unusual position of the cæcum, an abscess has been formed elsewhere in the abdomen, for the most part under the left rectus at the level of the umbilicus.

Finally, it must be mentioned that if the appendix is adherent to the iliacus-peritoneum, a perforation of it on the adherent side may lead directly to inoculation of and suppuration in the retroperitoneal tissue. And it may happen that in cases of long-standing perityphlitic abscess the iliacus-peritoneum may become secondarily necrosed and perforated. In either case, the pus gains entrance to the retroperitoneal tissue, and may burrow widely in it, baring the ilium, passing down into the thigh along the psoas, and even entering the hip-joint.

Certain complications may ensue in a case of perityphlitic abscess. A general peritonitis may be set up by rupture or leakage of the abscess, due to some movement of the patient, and this is most likely to occur at an early stage, when the protecting adhesions are soft. After the opening

of an abscess, fæcal matter may appear in the discharge for several days, and there is doubtless a communication either with the appendix or with the cæcum. This in nearly all cases soon closes, and no operative interference is advisable. The abscess, if neglected, may discharge spontaneously into the cæcum, or possibly into the rectum, and the result is not unfavourable. It may also open into the bladder, or through the abdominal wall. A fatal hæmorrhage has been known to occur from ulceration into an iliac artery after the opening of an abscess. An abscess in the liver may result, usually in long-standing cases, through an infective thrombosis of some radicle of the portal vein, either in the appendix itself, or more commonly in some part of the intestine which enters into the composition of the wall of the abscess cavity. The hepatic abscess is usually single, as in dysentery, and is amenable to surgical treatment, but sometimes a typical pylephlebitis results with the formation of ramifying channels of suppuration throughout the whole organ. The occurrence of intestinal obstruction by adhesions as a sequela of perityphlitis, simple or suppurative, is described elsewhere.

The prognosis in a case of perityphlitic abscess in the iliac fossa is extremely favourable if it is dealt with at an early period; but death occurs—perhaps in as many as 20 per cent. of the cases—either from neglect of the abscess, or from the difficulty of diagnosis and treatment, when it is situated in an unusual position, or from some one of the complications mentioned.

General peritonitis.—The onset of symptoms is, as a rule, sudden and severe from the first, and in only a small proportion of cases is there any previous history pointing to appendicitis. The signs and symptoms are for the most part identical with those of general peritonitis from other causes. There is a sudden onset of severe pain across the lower part of the abdomen, which is seldom more marked in the right iliac fossa than elsewhere. Vomiting occurs commonly within a few minutes or hours.

If the patient is seen within the first few hours, it is often impossible to recognise the true nature of the case, though the occurrence of a continuous abdominal pain with vomiting will always suggest the precaution of keeping the patient completely at rest. But during the first twenty-four hours the pain and vomiting continue, and perhaps increase in severity. The pain is constant, and not paroxysmal; the abdomen, which is acutely tender becomes more and more distended, and ceases to be moved during respiration. The temperature rises, and may reach 102° or 103°. The pulse is much quickened, the mouth and lips become dry, and the tongue is furred. The patient commonly lies on his back, with his knees drawn up. Before the second day is passed, the condition is usually clear. The pain and vomiting continue, though they may abate or cease under the influence of opium. Hiccough is sometimes distressing. The abdomen becomes more and more distended, and is absolutely motionless and very tender. It is often resonant in all parts, but in some cases at a later stage there is evidence of fluid in the flanks, and possibly elsewhere. The veins running down to the groins may become visible. Thirst and dryness of the mouth are distressing. The pulse is quick throughout, and becomes more and more feeble. The urine is scanty, and may contain albumin. There is often some pain in micturition, owing to the contraction of the bladder, of which the peritoneal surface is inflamed, and the use of a catheter is sometimes necessary. The bowels usually cease to act from

the first. The face is pinched and worn, and the eyes are sunken. As time goes on, the temperature may fall and may be normal or subnormal. The patient grows apathetic. The hands are cold and the forehead moist, the pulse can no longer be counted, and death occurs commonly about the end of the first week, though it is sometimes earlier by a day or two, and may be postponed for another week. Though death is the usual result, a small minority of cases, presenting all the signs and symptoms above detailed, end favourably. In many of these, as the general abdominal distension and tenderness pass off, some indication of an inflammatory mass can be felt in the right iliac fossa.

Certain variations in the onset and course of the illness are to be noted. In the first place, the onset may be gradual. The early symptoms are then of less severity, they are in fact not to be distinguished from those already detailed as occurring in a simple perityphlitis, and they may give rise to no anxiety. But they assume increased severity after the lapse of a few days, and a general peritonitis is rapidly developed, which will run the commonly fatal course. Such cases do certainly, though rarely, occur, even when the patient has been presumably kept in bed from the first, but they usually arise through a want of appreciation of the real gravity of the early symptoms, or through an attempt on the part of the patient to keep about or continue at work. In the next place, collapse may take place with surprising suddenness early in the illness, and, in the course of a few hours, a patient whose condition up to that time is not unfavourable may pass the point at which an operation can be undertaken. Finally, in some cases, a general peritonitis is suddenly developed by the rupture or leakage of a localised perityphlitic abscess, which may have been a week or more in existence. Such an accident, though decidedly uncommon, has been known to occur during the removal of a patient from his home to a hospital.

Prognosis.—In a simple perityphlitis recovery is invariable. In perityphlitic abscess the mortality rate is about 20 per cent., but there can be little doubt that this admits of considerable reduction. In general peritonitis of appendicular origin the mortality is very high, but even here a successful result after operation is becoming more common. The general mortality of all forms of peritonitis, due to disease of the appendix, may be placed at 10 to 12 per cent.

Treatment.—A correct treatment of appendicitis and the resulting peritonitis can be based only on a correct appreciation of the nature and extent of the changes which are taking place from day to day in the peritoneal cavity. Upon the appearance of the symptoms that have been detailed as marking the beginning of inflammation of the peritoneum, the patient must from that moment be confined to his bed, and arrangements must be made which shall obviate his rising for the calls of nature. The diet should consist mainly of milk diluted with soda-water, and beef-tea, meat-jelly, or the like. A grain of opium in a pill, or a quarter of a grain of morphine subcutaneously, may be given to an adult, and may be repeated in four hours' time. But it is of importance to be sparing in the use of opium, for the effect is often to produce a great though temporary improvement in the appearance and feelings of the patient, so that it is difficult to form that correct idea of his real condition upon which proper treatment must be based. Hot fomentations or an ice-bag will be found to give some relief from the pain.

From the early symptoms it is often impossible to foresee what

degree of peritonitis will result, whether it will be localised in the right iliac fossa or will become generalised ; and, as has been already mentioned, the first pain, even in a mild case of simple perityphlitis, is often felt as widely diffused over the abdomen as in a general peritonitis. But sometimes from the first, and generally during the first twenty-four or thirty-six hours, it can be determined with certainty whether the peritonitis will be local or general, and the further treatment will vary in the two cases.

Local peritonitis.—The diet must be fluid and light until a day or two after the temperature has become normal, and it may then be gradually increased in variety. The pain can be relieved to some extent by warmth or cold, and four or six leeches for an adult applied over the right groin will often prove of great service. Opium must usually be employed at first, but its use must be sparing, and it must be discontinued as soon as possible. The patient must be kept in bed, at any rate until several days after the disappearance of all tenderness and fever. No attempt should be made to procure an action of the bowels until evidence of the subsidence of the inflammation is perceived and it is always well to err on the side of constipation. At first, a glycerin or simple enema must be used, and no purgative should be given until the patient is well enough to leave his bed. During convalescence an occasional small dose of castor-oil or some mineral water is often required, and if mucus is found in the stools it may be well to give salol (15 grs. a day) for a week or so. For the rest, it is important that for some months the patient should not take any violent exercise, should be careful in his diet, and should not allow the bowels to become constipated.

All through the conduct of the case, the possibility of the formation of pus must be kept in mind. If the case is methodically observed from the first, there is usually little difficulty in recognising abscess formation. An abscess must be opened as soon as it is certainly recognised, but in cases of doubt it must be remembered that a delay of a day or two in the case of a patient who is under skilled treatment and nursing, is attended with no appreciable risk. When a perityphlitic abscess has been dealt with, and has healed, it is exceedingly rare for any further trouble to develop in connection with the appendix. A second abscess, however, has been known to occur after the lapse of three years.

On the other hand, after an attack of simple perityphlitis, subsequent attacks are very likely to occur, and a recurrence has been variously estimated as occurring in from 23 to 44 per cent. In many cases a long series of attacks will occur, so that the patient is more or less incapacitated for work or play, and he may become a confirmed invalid. While the attacks in such a case usually tend to become less and less severe, it must be remembered that any one of them may prove fatal. Consequently, on the ground of preventing the great loss of time and the slight loss of life that is entailed by a recurrence of attacks, excision of the appendix should be recommended to the patient after the first attack. The risk attending the operation is very slight. The most favourable opportunity for operation is the time when all fever and general symptoms have subsided, and the right iliac fossa is free from tenderness.

It is not possible to foresee in any individual case whether an attack will be a solitary one or the first of a long series, and consequently it may be thought advisable to wait for a second attack before recommending excision. But it must be remembered that every attack tends to leave

adhesions around the appendix, and in some cases the appendix becomes so firmly bound down that its removal cannot be carried through with safety. Indications which should more particularly point to operation after a first attack are the presence of a tangible enlarged appendix and the possibility of the occurrence of pregnancy.

General peritonitis.—The feeding and management of a patient in whom the peritonitis is becoming or has become generalised, are of great importance, but do not need any special description. Although some few cases recover without operation, even when the peritonitis, as judged by the physical signs, must be said to be general, yet in the majority of instances immediate operation affords the only hope of saving the patient, and it should be undertaken at once in all cases. The abdomen must be opened in the middle line, and also over the right iliac fossa, and an attempt must be made to excise the appendix, and at any rate, by flushing all parts of the peritoneal surface, to remove the inflammatory products which are teeming with micro-organisms. Even when this is carried out at the earliest moment, as thoroughly as possible, the mortality will still remain very high. There may be numbers of centres of infection or small collections of pus lying between the intestines in all parts of the abdominal cavity, and after the most thorough flushing many of them will remain untouched.

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H. P. HAWKINS.

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DISEASES OF THE LIVER.

THE liver of an adult weighs about $\frac{1}{36}$ of the weight of the whole body; at birth it is relatively larger, and weighs $\frac{1}{18}$. It has five surfaces. The anterior lies underneath the ribs, and is entirely covered by peritoneum, except for the narrow strip between the two layers of the falciform ligament. The superior surface is moulded to the diaphragm, and has on it a shallow concavity corresponding to the position of the heart. The posterior surface merges into the inferior; such of it as occupies the left lobe abuts upon the lesser curvature of the stomach; the rest of this surface is occupied by, from left to right, the Spigelian lobe, which is opposite the tenth and eleventh dorsal vertebræ, the depression for the inferior vena cava, and most to the right a strip of $2\frac{1}{2}$ to 3 in. broad, which is uncovered by peritoneum, and rests against the ascending part of the diaphragm, and has on it a slight depression formed by the right suprarenal capsule. The inferior surface looks downwards, backwards, and to the left. The part of it formed by the left lobe is moulded over the stomach. Passing from this to the right we find the quadrate lobe, which is in contact with the pylorus and the first part of the duodenum; next to the right we meet the gall bladder; and the large portion of the inferior surface to the right of this is in contact anteriorly with the hepatic flexure of the colon and posteriorly with the right kidney. The right surface lies in contact with the right lateral wall of the abdomen.

The liver occupies the right hypochondriac and epigastric regions, and often extends into the left hypochondriac and right lumbar. On deep inspiration in thin people, whose abdominal muscles are lax, the lower edge of the right lobe between the anterior and under surfaces can be felt by the fingers to descend, if they are thrust up under the ribs. In the

epigastric angle a small portion of the anterior surface of the left lobe comes in contact with the anterior abdominal wall, but it usually cannot be felt owing to the rigidity of the rectus. Except for this, the liver is everywhere separated from the surface by the ribs. Symington gives its relations as follows: The right surface is protected by the seventh to eleventh ribs, the anterior surface by the fifth to ninth costal cartilages, by the anterior parts of the corresponding ribs, and by the ensiform cartilage, the diaphragm being of course interposed. The upper limit may be indicated by a line which crosses at the lower end of the body of the sternum. To the left, this line passes horizontally; to the right, it ascends slightly, so that in the nipple line it is near the upper border of fifth rib; from this point it descends to the seventh rib in the mid-axillary line. The lower limit of the liver corresponds with the lower margin of the right ribs, as far towards the middle line as the tip of the ninth right costal cartilage; it then passes upwards and to the left to near the tip of the eighth left costal cartilage, and it is then continued upwards and to the left till it meets the upper limit at an acute angle. The precise relationship of the liver to the abdominal wall varies slightly in health, for the organ is often a little lower in the erect than the horizontal posture, and it descends on inspiration and ascends on expiration.

It is clear that much lung intervenes between the liver and the skin, and it is often of importance to remember that posteriorly the thin lower border of the lung does not reach lower than the tenth rib, so that below the tenth rib the costal and diaphragmatic portions of the pleura are in contact; and that the inferior limit of the pleura does not quite extend to the attachment of the diaphragm, but leaves a small portion of the circumference of this muscle in contact with the costal parietes.

The hepatic dulness to the left of the sternum cannot be distinguished from that due to the heart. On the right it begins at the end of the body of the sternum; in the nipple line it reaches the fifth intercostal space, in the mid-axillary the seventh, and in the line of the angle of the scapula the ninth, but its limit at the back is often difficult to determine precisely. In trying to settle whether the liver is enlarged, it should be remembered that in children it is proportionately larger than in adults; that when the chest is deformed from rickets or curvature of the spine, the liver descends lower than in health; that it may be thrust down considerably in women by tight-lacing, and in men by the practice of wearing a belt; or by extensive pleuritic or pericardial effusion; or by collections of fluid between the liver and diaphragm or in the substance of the diaphragm; and, lastly, in that rare condition known as Glenard's disease the liver may in the erect posture descend considerably. Tight-lacing may furrow it so deeply that the furrow can be felt during life. Ascites and any very large abdominal tumour may press the liver up so that the hepatic dulness is raised, and Murchison has recorded a case in which the liver passed into the chest through a congenital hole in the diaphragm. Extensive emphysema or a collection of gas in the abdominal cavity, such as occurs after perforation of the stomach, may obliterate the hepatic dulness. Various abdominal tumours may cause the liver to appear larger than it really is. When this deception arises from a mass in the omentum (and this is the commonest cause), the edge of the liver can usually be made out apart from the tumour, and a narrow line of resonance often intervenes between the two. Masses of fæces in the colon, and tumours of the stomach and of the kidney, may also

cause difficulty; and any of these abdominal tumours may from their attachment to the liver move during respiration. Confusion sometimes arises, because the colon gets in front of the liver. Lastly, tumours of the abdominal wall may lead to error.

The reflected pain and cutaneous tenderness due to disease of the liver are not as a rule referred so distinctly to definite cutaneous areas, as they may be when other organs are diseased; but Head considers that the eighth and ninth dorsal segments on both sides, and the tenth on the right, corre-spond to the liver. The eighth begins at the back opposite the ninth and tenth dorsal spine, and the ninth opposite the eleventh and twelfth; both extend nearly horizontally round, so that the lower margin of the ninth is at the umbilicus. The posterior maximum points of tenderness of each is almost vertically below the vertebral border of the scapula, the anterior maximum point of the ninth is just over the gall bladder, and that of the eighth is just above it. The tenth dorsal area is rather a wide one, lying below the ninth. The cephalic areas associated with these are the occipital, associated with the tenth; the parietal, with the ninth; the vertical, which is on the scalp just in front of and above the ear, with the eighth; and in hepatic disorders, headache and cutaneous tenderness may be present in these areas. In cases of gallstones and disease of the gall bladder, the reflected pains and cutaneous tenderness are often very well marked, especially over the eighth and ninth dorsal areas, but the fifth, sixth, and seventh are as a rule implicated more or less.

JAUNDICE.

Etiology.—Saunders showed, at the end of the last century, that jaundice could be produced by ligature of the bile duct; and even now the only form of jaundice we understand is that in which, owing to partial or complete obstruction to the flow of bile through the ducts, the rise in pressure behind the obstruction leads to an absorption of the bile—partly by the veins, but chiefly by the lymphatics—into the blood, from which it passes with the plasma into the tissues, which it stains. This is called obstructive jaundice; its causes are as follow:—

A. **Obstruction within the ducts outside the liver—**
1. Gallstones. This is one of the most common causes of jaundice.
2. Cancer of bile ducts
3. Cicatrix from a heated ulcer   } Very rare.
4. Congenital obliteration
5. Hydatid ruptured into the bile duct
6. *Ascaris lumbricoides*
7. Distoma   } Mere curiosities.
8. Foreign bodies passing in from the duodenum
9. **Thickening of bile.**—Probably the best instance of jaundice due to this is that seen in poisoning by toluylendiamine, which greatly increases the consistency of the bile, and it is supposed that it becomes so thick as really to obstruct its own flow.
10. **Swelling of the mucous membrane from inflammation.**—In this condition it is possible that the increased secretion of mucus thickens the bile, and so the obstruction caused by the swollen mucous membrane is increased. So strong is the belief that the condition commonly called simple jaundice is due to inflammation spreading from the duodenum into

the bile duct, that many call it catarrhal jaundice, but the post-mortem evidence of catarrhal inflammation of the bile ducts is very scanty.

11. Spasm of the ducts.—Severe fright or shock may cause jaundice, and this has been ascribed to a spasm of the duct.

B. Obstruction from pressure on ducts outside the liver—

1. Enlargement of the glands in the transverse fissure.—This is a very common cause of jaundice. The enlargement is nearly always due to malignant deposit, usually dependent upon growth in the liver or gall bladder. Lardaceous, gummatous, or tuberculous glands in the transverse fissure are mere curiosities.

2. Cancer of the head of the pancreas.—This also is a common cause of jaundice.

3. Growth of, or fæces in, the hepatic flexure of the colon
4. Enlargement of the kidney
5. Floating kidney
6. Aneurysm of hepatic artery
7. Other abdominal aneurysms } Very rare.
8. Peritoneal bands, thickenings, or tumours
9. Pregnant uterus
10. Ovarian or uterine tumours
11. Cicatrisation of a duodenal ulcer

C. Obstruction within the ducts inside the liver—

1. Cancer of the smaller bile ducts.

2. Thickening of the bile.—Many forms of jaundice have, on the strength of experiments with toluylendiamine, been ascribed to this; and some observers suppose that whenever the obstruction is not visible to the naked eye, as, for instance, in acute yellow atrophy, yellow fever, pyæmia, pneumonia, snake poisoning, phosphorus poisoning, cirrhosis of the liver, jaundice due to shock or fright and that due to arterial or venous congestion of the liver, the jaundice is really obstructive, the obstruction being the thickened bile in the minute ducts.

3. Hanot has suggested that some of the varieties of jaundice just mentioned may be due to swelling of the hepatic cells; he supposes that certain toxines may cause this, that it is unlikely that the swelling will be equal in all the cells, that if the cells at the periphery of a lobule are more swollen than those at the centre, the pressure of bile in the centre of the lobule will be raised, and that thus we shall have a form of obstructive jaundice.

D. Obstruction from pressure on ducts inside the liver—

1. Cancerous or sarcomatous nodules in the liver.
2. Abscess in the liver.
3. Hydatids in the liver.
4. Congestion of the liver.—A patient suffering from a nutmeg liver, owing to disease of the heart or lungs, is often jaundiced, and it has been supposed that this is because the distended veins press on the finer bile ducts.

5. Cirrhosis.—It is possible that the jaundice in this condition is partly due to pressure caused by the contraction of the new-formed fibrous tissue.

It has been thought that sometimes jaundice may be caused by the obstruction to the flow of bile, which would result from imperfect respiratory movements. That associated with pneumonia might be due to this

cause, but it is probably toxic. It will be seen from the above list that it is possible to explain all cases of jaundice, on the supposition that they are due to obstruction to the egress of bile, and its consequent excessive reabsorption. All pathologists admit this explanation, when the obstruction is obvious after death, and many think no other form of jaundice is possible. But other explanations have been suggested for those cases in which the obstruction is not obvious.

Some suppose that the process of secretion is at fault. Too much bile may be secreted, or it may contain too much pigment, or some abnormal pigments which are easily absorbed; and it is further supposed that, under these conditions, reabsorption of bile may take place in the ducts, without any increased pressure in them, or it may take place from the intestine. Another view is that of Liebermeister, who suggests that the liver cells may be diseased in such a way that they cannot sufficiently rapidly excrete all the bile they form, and so some of it is reabsorbed from them.

Many believe that in some cases jaundice is the result of a change in the blood. Thoma has recently supported this view. Certain persons, he points out, can separate the hæmoglobin from the corpuscles; it becomes free in the blood; some of it passes out in the urine as methæmoglobin; and another part, he believes, reaches the liver, and is converted into bile pigment. Thus an excess of bile is excreted, this excess is absorbed from the biliary passages and intestines, and so the jaundice exists. He also suggests that, in some cases, bile pigment may be formed in the tissues from the blood; and he quotes Neumann as saying that bile pigment forms in blood extravasated into the tissues.

Clinically it is always important to determine whether jaundice is due to some gross obstruction of the larger ducts, and to remember that nearly all cases of jaundice are due to malignant disease, gallstones, catarrhal jaundice, or cirrhosis.

Symptoms.—In health, neither bile acids nor pigment can be demonstrated in the blood, although they are probably reabsorbed from the intestine. The failure to find them is due most likely to their rapid excretion by the liver and kidneys. When, however, the patient is jaundiced, they are present in the blood, and they produce the following symptoms, the first mentioned being due to bile pigments:—

The skin is yellow, owing to the staining of the Malpighian layer by the bile pigment, which has diffused out of the blood vessels. The tint, which often appears within twenty-four hours of the onset of obstruction, varies from a faint to a deep bright yellow; if the pigment is not quickly reabsorbed from the skin, the colour gradually becomes deeper and green, until it is finally a very dark olive; but this dark tint is only attained when the jaundice is obviously obstructive, and has lasted some time. All jaundice may vary in intensity from day to day. Slight jaundice is easily confounded with the tint of skin often seen in anæmia; but if the patient is genuinely jaundiced, the conjunctivæ are always stained, but care must be taken not to mistake fat in them for bile pigment. Slight jaundice cannot be detected by artificial light. The yellowness of the skin often persists long after the cause of the jaundice is removed; this is probably because the excess of bile in the blood is excreted by the liver, and reabsorbed from the intestine. The visible mucous membranes are rarely stained, but the tongue may be slightly yellow.

The urine contains a considerable amount of both bile pigments and acids. The former give it a dark yellow tint when seen by transmitted,

and a green lustre when seen by reflected, light. Any froth on the surface of the urine is bright yellow. The usual test is for a little urine on a white plate to be allowed to come in contact with a little strong nitric acid; if bile pigments are present, the colour changes at the line of contact, becoming green, blue, violet, red, and lastly yellow. If to some nitric acid in a test tube some jaundiced urine be added slowly with a pipette, a red layer is seen at the line of junction, and above it green, blue, violet, red, and finally green layers. These tests show better if the bile pigment be dissolved out of the urine with chloroform; but a delicate test for the presence of bile in the urine is much wanted, because often the nitric acid test is only decisive when to the naked eye it is obvious the urine contains bile. Such urine frequently stains the bedclothes yellow. Pettenkofer's test is recommended for bile acids, but it is very unsatisfactory. Clinically, the dark urine of jaundice has to be carefully distinguished from that in which the coloration is due to drugs, such as santonin, rhubarb, or senna.

The sweat is usually uncoloured, but it may be stained a little. The saliva is never coloured, unless, as in mercurialism, the secretion is pathological. The tears are always free. The milk may contain bile pigment, for infants have been known to become jaundiced when at the breast of a jaundiced woman. As a rule the sputum is unstained, but if the patient have pneumonia or bronchitis it may be yellow. Ascitic and pleuritic fluids are often jaundiced.

The following symptoms are most probably due to the presence of bile acids in the blood. Disintegration of the red corpuscles, and the presence of dissolved hæmoglobin in the blood increases the formation of bile pigment by the liver, and thus deepens the jaundice; the blood destruction often leads to general weakness and anæmia, and is very likely the cause of great liability to petechial or even the more serious hæmorrhages which may often be seen in cases of long-standing jaundice. There is often a bitter taste in the mouth; this is perhaps due to taurocholic acid. Pruritus may be very distressing, and render the patient's life unendurable. It usually only occurs in cases in which the bile duct is obstructed. In most cases the only remedy is the subcutaneous injection of morphine. The rate of the pulse is often reduced; sometimes it is as low as 40, 30, or even lower. Cerebral symptoms are not rare in cases of long-standing jaundice, and they often close the scene. The most common are depression of spirits, stupor, and coma, and the patient may lie in a dull lethargic condition for days or weeks. But, as in the last case under my care, he may have acute delirium, wild maniacal excitement, and convulsions. Rarely he sinks into a typhoid state. Xanthopsy, or yellow vision, is very rare. I have only once met with it. Possibly it is due to staining of the media of the eye.

Certain other symptoms do not obviously fall under the heading of poisoning by either bile pigment or bile acids. When the bile cannot reach the intestines, the bowels are constipated, the fæces are clay-coloured, contain much fat, stink horribly, and the patient suffers from indigestion and flatulence. Those affected with jaundice occasionally suffer from xanthelasma, for a description of which the reader is referred to the chapter on diseases of the skin. Lichen urticaria and boils are also mentioned by Murchison, but they are very rare. It is said that jaundice diminishes the glycogenic function of the liver, and this may help to explain the wasting seen in long-standing cases.

On post-mortem examination, the subcutaneous tissues, the connective tissues generally, and the liver, are deeply stained. The kidneys, muscles, tendons, bones, pleura, and peritoneum show the staining less; and the brain, spinal cord, nerves, salivary gland, and pancreas do not show it at all.

In certain diseases, such as catarrhal jaundice, acute yellow atrophy of the liver, phosphorus poisoning, nervous jaundice, and icterus neonatorum, the jaundice is so striking that they are described from the standpoint of it.

CATARRH OF THE COMMON DUCT.

This common disease is named from its most prominent symptom. The term catarrhal jaundice has been applied, on the supposition that there is a catarrhal swelling of the mucous membrane of the common duct at its entry into the duodenum, and that it becomes obstructed partly by the swelling, and partly by a plug of thick mucus. The inflammation is supposed to spread from the duodenum. This hypothesis is supported by Dupré, who has described all the histological characters of catarrhal inflammation as occurring in the common duct in catarrhal jaundice. Osler, too, has seen a plug of inspissated mucus filling the diverticulum of Vater, and the narrower portion of the duct just at the orifice, but it must be admitted that our knowledge of the cause of this form of jaundice is very scanty. Probably, if there is any catarrh, it is due to a micro-organism. On this view catarrhal jaundice is an obstructive jaundice, but it has been suggested that toxines produced by gastro-intestinal catarrh may be absorbed by the portal vein, and in some way so act on the liver as to cause the jaundice.

Etiology.—Usually no cause can be assigned, but simple jaundice may follow indigestion, and probably is often consecutive to gastric catarrh induced by indigestible food. It is much commoner in the young than the old, and according to some is frequent in the autumn and spring. Occasionally at these seasons so many cases may be seen, that they suggest an epidemic influence, and sometimes undoubted epidemics occur. Murchison considers that simple jaundice may be a symptom of secondary syphilis, and he thinks that in elderly persons it may be due to gout; still it is very important for the student to remember that the jaundice of elderly people is rarely simple.

Symptoms.—Any of the symptoms due to bile circulating in the blood may be present in catarrhal jaundice. The discoloration of the skin is very marked; it is bright yellow, but never dark green. Pruritis is rarely severe, and the only cerebral symptom is a feeling of intense depression. The motions are clay-coloured, and the bowels are constipated. The attack is usually preceded or accompanied by symptoms of gastric catarrh, namely, pain and epigastric tenderness, nausea, vomiting, loss of appetite, and a furred tongue. The liver may be a little enlarged and tender, and the gall bladder, being distended, may be easily felt. Very rarely there is slight pyrexia. The patient commonly only feels ill for a few days or perhaps a week, but the jaundice is slow to go, and some remains after the patient is otherwise quite well; cases are indeed recorded in which it has lasted two or three months. The disease is liable to recur in the same patient, but usually it completely disappears, and it is never fatal.

Treatment.—The patient should remain in bed a few days. His

food should be light and easily digestible, usually farinaceous articles are to be preferred. The bowels should be kept open once a day, and some mild cholagogue purge, such as a little calomel at night, followed by a sulphate of sodium mineral water in the morning, is perhaps the best. Occasionally, if there is much hepatic pain, hot fomentations are soothing. Should syphilis or gout be present, the patient may have mercury or colchicum.

ACUTE YELLOW ATROPHY.

This disease is rare, but is apparently commoner here than in America; for Osler has never seen a case, while I have come across four.

Etiology.—Seventy per cent. of the cases occur in women, and of these about half are pregnant when the disease first shows itself. Nearly all the patients are between the ages of 20 and 40. Perhaps cirrhosis of the liver predisposes to acute yellow atrophy. The affection is probably of toxic origin.

Morbid anatomy.—The size of the liver varies, but it is nearly always atrophied; and we have one in the museum at Guy's Hospital which, in the recent state, weighed only 19 oz. That of the last case under my care weighed 31 oz., and somewhere near this is a very usual weight. The capsule is nearly always healthy. The liver is equally diminished in size in all directions, and so soft and flabby that it easily folds on itself. Looked at from the outside, it is usually of a dirty greenish colour; but on section three kinds of large patches of colour are seen—bright yellow, deep red, and the ordinary hepatic colouring. If the case has been very short, the yellow is in excess; if the patient has lived longer than usual, the red is more extensive; and this, taken with the fact that the red parts may apparently shrink and cause depressions on the surface of the organ, goes to show that they represent a later period of the disease than the yellow. Histologically, the yellow parts show only granular débris, the substance of the liver having evidently undergone rapid destruction. In the red patches there is, in addition to these changes, some increased fibrous tissue in connection with the vessels around the lobule. There may be a slight excess of fat, and there are many crystals of leucin and tyrosin. Occasionally, acute yellow atrophy appears to follow cirrhosis of the liver, or the formation of gallstones. The muscles, especially the heart, and the kidneys are in a state of fatty degeneration, and the tissues may be stained yellow. Hæmorrhages are common. Leucin and tyrosin may be seen in the kidney.

Pathology.—The whole behaviour of acute yellow atrophy of the liver points to its being due to a micro-organism. Staphylococci, streptococci, the *B. coli communis*, and a diplococcus, have all been described as being present, but no definite micro-organism has yet been isolated.

Symptoms.—To obtain a conception of the disease, the reader should picture to himself a woman desperately ill, in the typhoid condition, of a light yellow colour, and with many subcutaneous and other hæmorrhages. I have known a case of severe pyæmia mistaken for acute yellow atrophy.

The onset varies: the patient may be suddenly seized with a rigor, and quickly become very ill, with headache, backache, great prostration, vomiting, fever, and in a few hours jaundice; and, to show how sudden the onset may be, I may mention that I have known a case, thought to be pneumonia, with jaundice, turn out to be acute yellow atrophy. But she

may not seem dangerously ill, or even be jaundiced, for four or five days; and sometimes the disease is preceded by marked symptoms of indigestion. The jaundice is never very deep; indeed, Boix says it may be absent. Its depth bears no relation to the intensity of the disease. Bile is always present in the stools. There is usually pain and tenderness in the hepatic region, and, unless emphysema or some other source of error makes it difficult to obtain an exact idea of the size of the liver, careful percussion will show that the organ day by day diminishes in size, until the hepatic dulness is, perhaps, not more than a third of its normal width; but it must be remembered that in the early stages of the disease the organ may be slightly enlarged, and that the patient may die before the atrophy has proceeded far. The spleen is slightly enlarged, and may be tender; the tongue is dry and brown; there is often much blood about the mouth, and this makes the breath very foul. Vomiting is often troublesome, and the vomit may be black from altered blood. Sometimes there is constipation, at others diarrhœa; the motions may contain blood, and may be passed into the bed. The pulse is rapid, unless the jaundice is so deep as to slow it, soft, very feeble, and often irregular; there is considerable dyspnœa, and the respirations are rapid, out of proportion to the temperature; indeed, there can be little doubt that some toxic product is present in the blood, which is a powerful cardiac and respiratory depressant. The nervous symptoms collectively known as the typhoid state, are very striking. The patient lies prostrate on her back, in a state of low, muttering delirium, which is rarely violent, and is more marked at night. Fine fibrillary tremors may be seen in her muscles, she picks at the bedclothes, and subsultus may be noticed. Although dulled and lethargic, she is, till towards the end, continually awake; but then coma gradually supervenes. She becomes immobile, the cornea are insensitive, a sweat breaks out on her face, and finally death ends the scene. Convulsions are rare. Bleeding may occur almost anywhere, but is most common under the skin, from the nose, or from the uterus. If pregnant, the patient usually miscarries. The temperature is very variable; sometimes it is raised a few degrees, but often it is subnormal.

The patient usually passes her urine under her; it is scanty, high coloured, and of a high specific gravity; it contains a few granules and hyalin casts, usually some albumin, and perhaps blood. Very little bile pigment may be present in it, and it is usually impossible to detect any bile acids. The striking thing is the great diminution of urea, and the presence of stellate sheaves or globular masses of crystals of tyrosin, and rounded laminated crystalline masses of leucin. These are generally quite easy to detect with the microscope, especially if the urine is centrifuged; they become more abundant as the disease progresses, and are diagnostic of acute yellow atrophy. The salts of the urine are diminished. The patient is usually dead within a week of the onset of the severer symptoms, but a few cases of recovery are recorded.

Diagnosis.—Acute yellow atrophy is almost certainly a definite disease. The points of difference from yellow fever, malaria, typhoid fever, pneumonia, pyæmia, typhus, scarlet fever, and relapsing fever are mentioned under these headings. In all these conditions the liver may become very fatty, but a fatty liver does not resemble that affected with acute yellow atrophy, and although Murchison states that crystals of leucin and tyrosin may be found in the liver and kidneys when they have undergone fatty degeneration, this is certainly quite exceptional. Epidemic

jaundice and Weil's disease are little understood, but their whole course marks them off from acute yellow atrophy; and the same is true of the jaundice induced by poisons, such as snake poison. Other poisons which will cause jaundice are the fungus known as *Helvella esculenta,* male fern, toluylendiamine, glycerin, chloroform, ether, pyrogallic acid, and naphthol. Phosphorus is a sufficiently common poison to deserve separate mention. For the first few hours after taking it there are no effects. Then abdominal pain, nausea, and vomiting set in. The vomited matter often smells of phosphorus, and is luminous in the dark. There is some collapse, but these symptoms usually pass off, and the patient soon appears much better. But in three or four days, jaundice, which soon becomes deep, is noticed, and the liver may be a little enlarged. There is intense prostration and great thirst, the skin is cold, the pulse feeble and rapid. Vomiting of blood and bloody diarrhœa may be observed, but these two symptoms are not severe. The urine, which is scanty, high-coloured, albuminous, bile-stained, and perhaps bloody, may contain crystals of leucin and tyrosin. Muscular twitchings are noticed, and the patient dies comatose. At the post-mortem there is general fatty degeneration, affecting principally the liver, which may be extremely fatty, but it never looks as though it were affected with acute yellow atrophy. Hæmorrhages in most of the organs of the body are common.

The *brown atrophy* of Wilks and Moxon, called chronic atrophy by Frerichs, and red atrophy by Rokitansky, must be sharply distinguished from acute yellow atrophy, to which it bears no relation. The liver is atrophied, it may weigh only 24 oz., it is flabby, and varies from dark brown to red. The cells are atrophied, and often ruptured; the ramifications of the extremities of the portal vein are destroyed, so that the minute branches of it end in blind extremities, and the organ cannot be injected from it. There are symptoms during life of obstructed portal circulation, but the condition is so very rare that we know very little about it.

Prognosis and treatment.—These patients rarely recover. The only treatment is to maintain their strength.

ICTERUS NEONATORUM.

Newly-born children are liable to many forms of jaundice. The commonest, which is most often seen in foundling hospitals, appears two or three days after birth, and disappears within two or three weeks. The child does not appear very ill. The urine may contain bile; the fæces are pale. The cause of this variety of jaundice is not known.

There is also a very rare severe form, which is usually fatal in a few days, and is often accompanied by hæmorrhage from the umbilical cord. The jaundice is very dark, the child suffers from diarrhœa, hæmoglobinuria, pyrexia, and finally coma, and perhaps convulsions. This variety is probably due to septic infection through the umbilical cord. The kidneys usually show acute nephritis, with many hæmorrhages in their substance.

Jaundice in the new-born may also be due to congenital obliteration of the common duct, to syphilitic disease of the liver, and in very rare instances to a calculus. It is said that new-born children may suffer from " catarrhal jaundice."

NERVOUS JAUNDICE.

Although this is rare, there is no doubt that it exists. Many instances in which some severe fright or emotion caused jaundice occur in medical literature, as, for example, that of a man who became jaundiced just before he was about to fight a duel. I have heard of the case of a child who became jaundiced when she saw her sister accidentally drowned. The cause of the jaundice in these cases is unknown. It passes off, and no special treatment is necessary.

GALLSTONES.

Etiology.—The origin of gallstones is very obscure. Several observers, working under the direction of Naunyn in his laboratory at Strassburg, have shown that the amount of cholesterin in the bile is quite independent of the quantity of this substance in the food, nor is it influenced by any alterations in diet, by any particular disease, or by the quantity in the blood. Naunyn points out that the secretion from diseased mucous membranes often contains considerable quantities of cholesterin, and as this substance is always increased in the bile from which calculi are deposited, he suggests that the formation of gallstones may be partly due to the excess of cholesterin which follows disease of the mucous membrane of the biliary passages. As a proof of the importance of the secretion of cholesterin from the biliary mucous membrane, we may mention that stones may be found in diverticula, or pockets of the biliary passages, which have evidently been quite shut off from the passages, and therefore from the bile, for some time, although microscopic examination shows that the stone was continually growing. It will be remembered that the other chief constituent of calculi, besides cholesterin, is bilirubin-calcium; and therefore it is important to bear in mind that the quantity of calcium in the bile is quite uninfluenced by the diet, but that the mucus secreted by a diseased mucous membrane contains lime. It seems possible, therefore, that the reason why women suffer from gallstones so much more frequently than men, is that the habit of tight-lacing damages the gall bladder, the mucous membrane of which, therefore, secretes considerable amounts of cholesterin and calcium. But these facts will not completely explain the formation of gallstones, for Happel has published some tables which show that cholesterin is soluble to the extent of 5 per cent. in olein, and also (although to a considerably less extent) in soaps, and glycocholate and taurocholate of sodium; and that all those substances are present in human bile in ample quantity to keep in solution, at the body temperature, all the cholesterin it ever contains; and although the decomposition of the glycocholic and taurocholic acids will to some extent diminish the power of the bile to hold in solution the cholesterin, still this diminution is not great enough to be important; and therefore we must conclude that the formation of a gallstone cannot depend upon mere excess of cholesterin; and, further, we learn that crystals of it, seen in the bile at a post-mortem, must have separated out after death, probably owing to the cooling of the body. These facts suggest that cholesterin, before it can form a gallstone, must be precipitated about some body acting as a nucleus; although epithelial cells can be seen floating in bile, even when no gallstones are present, Naunyn brings forward much

evidence to show that, when these cells have undergone fatty degeneration, they can themselves form cholesterin, and further lead to the aggregation around them of amorphous cholesterin (which later becomes crystalline) and bilirubin-calcium from the bile. The deposition of bilirubin-calcium is favoured in another way, for although human bile also contains an abundance of lime salts and bilirubin, and may even be artificially concentrated without any precipitation of bilirubin-calcium, certain albuminous substances greatly favour the precipitation of this substance, and it may well be that epithelial cells or an albuminous secretion from the mucous membrane of the biliary passages in this way help the precipitation of the bilirubin-calcium constituent of a gallstone. A biliary calculus is first a soft minute mass, which may be moulded by the gall bladder, and several of these masses may stick together. Then, if the calculus is to become hard, a crust of the chief constituent forms on the outside, and in the inner side of this the harder part of the soft contents are deposited, leaving, if there is sufficient soft material, a little collection of the fluid in the centre. In this way it is easy to understand how some stones may be solid throughout, others may be hollow, some may be soft, others hard. The further growth of the stone takes place by deposition from without, if the bile can reach it, of both bilirubin-calcium and cholesterin; but if the cystic duct is blocked, only cholesterin, secreted from the mucous membrane, will be precipitated. The lamination of the deposits probably depends upon the fact that, owing to temporary blocking of the cystic duct, sometimes no bile reaches the stone. It is of interest, in connection with this subject, to note that the introduction of foreign bodies into the gall bladder does not lead to the precipitation of cholesterin or bilirubin-calcium around them to form a gallstone; indeed, gallstones introduced into a dog's gall bladder undergo slow solution there.

The frequency of gallstones bears upon their etiology. The most recent investigations on this point are those of Schröder, who examined all the patients dying in the Strassburg Hospital, which contains both a children's department and an infirmary. He found that 12 per cent. of all the bodies examined contained gallstones, distributed as follows among the different decades:—Under 20 years, 2·4 per cent.; between 20 and 30 years, 3·2 per cent.; between 30 and 40 years, 11·5 per cent.; between 40 and 50 years, 11·1 per cent.; between 50 and 60 years, 9·9 per cent.; over 60 years, 25·2 per cent. 4·4 per cent. of the male and 20·6 per cent. of the female bodies examined contained gallstones, and they were much more frequent in those women who had borne children than in those who had not. These figures suggest that both pregnancy and tight-lacing favour the formation of gallstones, which are indeed especially often seen in women on whose livers the groove which shows tight-lacing is evident. Both prevent the free flow of bile, because they hamper the movements of the diaphragm, which greatly aid the biliary flow; and a floating right kidney, which is so much commoner in women than men, may by its compression of the bile ducts also hamper the flow. Mitral disease, as shown by Brockbank, is a cause. Lastly, the sedentary life led by women predisposes to stagnation of the bile. This last cause is especially operative in old age, in which, too, as Charcot has shown, the plain muscle of the biliary passage undergoes atrophy; and, further, it is only probable that the epithelium of the gall bladder will be more likely to be diseased in the old than in the young. Neither diet, locality, occupation, social position,

hereditary influence, or gout have any special influence on the formation of gallstones.

Healthy bile is sterile, but Naunyn considers that stagnation of it favours the growth in it of the *Bacillus coli communis.* This micro-organism may, he suggests, lead to the diseases of the mucous membrane of the gall bladder, which induces the formation of the stone. This is a more probable supposition than that the stagnation of the bile causes the inflammation of the mucous membrane (cholangitis), for the cause of the stagnation is usually more or less permanent, while the invasion by the bacterium might be transitory; and when many gallstones are present, not only are they of the same composition, but they appear to be of the same age. It is, however, by no means proved that the *B. coli* is the sole cause of gallstones, for Gilbert, examining the bile in thirty-six cases of gallstones in which an operation was performed, found living *B. coli* in twelve and dead *B. coli* in two; but it must be remembered bacilli might start the formation of a gallstone and subsequently die.

The influence of carcinoma is uncertain. It is common to find gallstones present when the gall bladder is carcinomatous, and it may be that some mass of carcinoma, by pressure on the duct, has led to stagnation of the bile, and that then the *B. coli communis,* setting up some cholangitis, has led to a gallstone; but, on the other hand, many authors consider that the gallstones are in these cases the cause of the carcinoma. The minute bilirubin-calcium calculi found in the substance of the liver are more common when that organ is diseased than when it is healthy.

From the facts just given, it will be seen that it is supposed that, in some cases at least, the *B. coli communis* sets up cholangitis; this leads to shedding of the epithelium, which forms a nucleus for the stone, and to an increased formation of cholesterin and bilirubin-calcium, which are precipitated on the nucleus, and the whole process is aided by a retardation of the flow of bile. It has been suggested that other micro-organisms, especially the typhoid bacillus, may cause gallstones, but the evidence is very slender. Sufferers from gallstones do not give a history of typhoid fever oftener than other people.

Morbid anatomy.—Biliary calculi, or gallstones, may be found either in the gall bladder, the cystic duct, the common duct, the hepatic duct, or the liver itself. They are far more commonly formed in the gall bladder than elsewhere, and from these are often forced into either the cystic or the common duct.

Cholesterin and bilirubin-calcium are the most important constituents of gallstones; calcium-carbonate, although frequently present, is usually found only in small quantities. Occasionally biliverdin, bilicyanin, bilifuscin, and bilihæmin are met with, and they too are nearly always combined with calcium. Minute traces of copper and iron are often mixed with the bilirubin-calcium. In quite exceptional instances metallic mercury, calcium sulphate, and calcium phosphate have been found, and traces of free bilirubin and the salts of the bile acids may soak into the stones from the bile.

Gallstones are most frequent in the gall bladder, and they are usually about the size of a pea, seldom larger than a cherry, and often quite small, it may be so minute that a number of them form a sort of sand. When very small they are rounded, but when larger they are usually faceted, because at first they are soft, and as commonly more than one is present, contiguous gallstones become pressed against each other. If they are still

soft when the patient dies, they may be crushed in the hand, but most often the central part only is soft, and is surrounded by a hard shell of varying thickness. Their colour is usually brown, yellow, or white, or some mixture of these colours. On section of the stone, it will be seen that some parts are darker than others, they feel soapy, the cholesterin in them may glitter, and there may be a central cavity containing a yellowish alkaline liquid. Any number, from one to many thousands, may be seen in one gall bladder, but in the same patient all the gallstones always have the same constitution and appearance.

In comparatively rare cases the gallstone may be larger than a cherry, and sometimes they may be as big as a hen's egg. These large stones are usually solitary, and therefore rarely faceted. They almost always lie in contact with the wall of the gall bladder, and may even entirely fill it. In the exceptional instances, in which more than one large stone is present, a distinct crepitus may sometimes be felt during life, if the hand is placed firmly over the gall bladder. Occasionally stones grow to a larger size in the cystic or in the common duct; and wherever it is, a stone may form a sacculus for itself.

Sometimes one constituent of a gallstone preponderates to such an extent, that the stone differs in appearance from the common stone, which is composed of cholesterin and bilirubin calcium, and has just been described. Naunyn draws up the following list of these rarer stones:—(a) Pure cholesterin stones. These are hard, rounded, non-faceted, large, and nearly always white, translucent, and smooth. They contain hardly anything but cholesterin. On section, they are white and crystalline throughout, without any signs of stratification. (b) Laminated cholesterin stones. In form and size these resemble those of pure cholesterin. They may be almost any colour, rarely they are soft and faceted. When cut they show a more or less crystalline structure, with alternately white and dark laminæ. They consist for the most part of pure cholesterin, and may contain 90 per cent. of it. (c) Mixed bilirubin-calcium calculi. These too contain cholesterin, but in much smaller quantity, although it may occasionally form 25 per cent. of the stone. They are mostly large, and may be faceted. The nucleus consists of cholesterin; outside this are broad laminæ, very liable to flake off, and consisting chiefly of bilirubin-calcium with some cholesterin. (d) Pure bilirubin-calcium calculi. These contain the merest trace of cholesterin, but a large amount of bilirubin-calcium with varying quantities of the calcium compounds of other biliary pigments, especially bilihæmin. These stones vary in size from a grain of sand to a pea, and are usually rough and irregular. They are grey or blackish brown, and often as soft as wax, although they may be hard and brittle; their shape is most irregular, and they may have processes on them. (e) Amorphous, or incompletely crystalline cholesterin calculi. These are quite small, and look like pearls. (f) Calcium carbonate occasionally forms the chief ingredient of gallstones. (g) Compound calculi. Sometimes it is quite evident, on cutting into a calculus, that a small calculus of one variety has formed the nucleus for one of another variety. (h) In cattle, casts—either solid or tubular—of the bile ducts may occur. They always consist of pure bilirubin-calcium. Casts are very rare in man. (e) (f) (g) (h) are all extremely rare.

Symptoms.—In considering these, we must bear in mind that, in the first place, gallstones are often found in the bodies of those who during life showed no symptoms of them; and, secondly, that there is no satisfactory evidence that they ever become dissolved.

It appears that gastro-intestinal contractions may set up contractions of the gall bladder or ducts, and so lead to an attack of biliary colic, for this often appears to be induced by irritating articles of diet. It is obvious that the severity of the colic will depend upon the force of the contractions behind the stone, the expansibility of the ducts, the shape and consistency of the calculus, and the pressure of bile behind it. This last is probably unimportant, for the bile is secreted at such a very low pressure. The narrowest part traversed by a stone is the cystic duct and the opening of the common duct into the duodenum; stones are therefore most frequently impacted in these situations.

Attacks of gallstone colic come on rather more frequently at night than in the day, and are sometimes preceded by slight premonitory symptoms, resembling those of the fully-developed attack, and these are very likely due to the passage of biliary gravel. The great and leading feature of an attack is agonising pain in the right hypochondrium, which usually comes on suddenly. Women often say that labour pains are not so severe as those of gallstone colic. The patient writhes in agony, and generally applies to the pain the same terms—stabbing, cutting, and boring—as are used by sufferers from intestinal colic. It commonly radiates through to the back and often to any part of the abdomen; and in extreme cases into the upper part of the thorax, the head, the arms, or even the right thigh. It is not so frequent in the right shoulder as other diseases of the liver would lead us to expect. Usually it lasts a few hours, but it may endure for days; occasionally it ends quite suddenly, but more commonly, although it suddenly becomes much less considerable, pain and discomfort last for some time. It must not be imagined that all attacks are as severe as this: there are all grades, from that just described to a mere sense of discomfort in the region of the gall bladder; and there is, I think, no doubt that many pains in women set down to indigestion are really due to biliary colic.

Vomiting is almost as common as pain. It is usually severe and frequently repeated, and the patient continues to retch after the stomach is quite empty. The pressure of the abdominal muscles which empty the stomach, helps no doubt the passage of the gallstone, and is also the cause of such a thorough emptying of the ducts, that bile regurgitates through the pylorus, and consequently the vomit is usually green. Even gallstones may pass into the stomach, and be found in the vomit. If the stone is irregular, some bile is probably pressed past it.

Jaundice is the next most common symptom, occurring in a half to three-quarters of all the cases. It is first noticed after the onset of the pain, and is in a few hours quite deep. After the pain has ceased, the bile rapidly disappears from the urine; but the staining of the skin and conjunctiva will, if it has been at all deep, remain many days. The stools are often of a light colour, but the obstruction to the flow of bile must be complete and last some time for these to be quite clay-coloured. As might be expected, any of the symptoms due to retention of bile from any cause may be present. They will be found described under the heading of "Jaundice"; of them a feeling of intense depression, a slow pulse, and constipation, are the most common. The abdominal muscles in the neighbourhood of the gall bladder are often rigidly contracted, and this may be a valuable aid to the diagnosis when the other symptoms are obscure. Occasionally the patient complains of painful cramps in various parts of the body.

The edge of the liver is very commonly painful; and even when the

organ is not enlarged, if the hand be placed under the ribs, severe pain is felt on deep inspiration, but often the swollen organ is easy to feel below the ribs, and if the attack lasts some time its edge may extend to a point midway between the costal margin and the umbilicus. In many cases the gall bladder is enlarged, and then it is often tender. It is felt as a rounded swelling at the outer margin of the right rectus, just under the ribs. It may enlarge even when bile cannot reach it, owing to complete obstruction of its own duct; then the distension is due to the secretion of colourless mucus.

The irritation of the gallstone occasionally causes the temperature to rise, it may be to 104°, or even more. It mounts very quickly, and does not remain up long. The height does not bear any necessary relation to the pain, and often the pyrexia is accompanied by a rigor. This shivering and pyrexia must be carefully distinguished from that due to suppuration in the liver or bile passages, or to ulceration of the biliary passages; then the rises of temperature are frequently repeated.[1]

Occasionally a little albumin is found in the urine. If the attack is very severe, or the patient very old, there may be much collapse—even fatal—with a feeble pulse and considerable sweating. If this or the vomiting are excessive, the patient may be very thirsty, and commonly she completely loses her appetite.

The motions passed after an attack should always be searched for stones, and the quest should not be given up for at least a fortnight. The motion should be thrown upon a hair sieve, and then slowly washed with water. Often no stone is found, and then it has usually become dissolved in the intestine; this nearly always happens to bilirubin-calcium calculi; in fact it is almost invariable that a stone passed per rectum is very hard, and consists chiefly of cholesterin. In exceptional cases the stone remains embedded in the duct, which, however, dilates enough to let some bile past, or still more rarely it may slip back into the gall bladder. Sometimes a great many—it may be over 200—are found in the same motion, or in a few motions passed closely upon each other. Should a very large stone be found in the intestine, it is clear that it can only have got there from ulceration into the gut. Probably no stone much larger than a cherry can pass by the natural passages. In concluding this account of the symptoms, I would again remind the reader that the attacks vary in severity, from a slight pain to a continual series of attacks spread over weeks; that even sometimes the pain may be absent; that when a patient has had one attack she nearly always has others; that repeated attacks of jaundice are almost diagnostic of gallstones, and that the prognosis is almost invariably good; and, lastly, that however severe the contractions, rupture of the gall bladder from this cause is one of the rarest events known.

Complications.—The presence of a gallstone may lead to many complications, which will be described under the following seven principal heads, less important complications being mentioned incidentally. For any of them it is almost necessary that the stone should be impacted, and therefore it follows that they are all usually secondary to the presence of large stones either in the cystic duct or at the duodenal end of the common duct; and it must be remembered that the stone can probably increase in size after it has become impacted.

[1] It will be noticed that these symptoms are of very short duration compared to the prolonged similar symptoms described as infective cholangitis on p. 765.

Simple impaction.—In extremely rare cases, which almost always give a history of repeated attacks of biliary colic, in each of which the jaundice is more severe than in former attacks, although the pain commonly gets less and less, till at last there may be none, a stone may remain impacted for some time without producing any of the evil effects just mentioned; and if it is fixed in the cystic duct, not even jaundice results; and if it is tight in the hepatic or common ducts, enough bile may very exceptionally pass it for the patient not to be jaundiced. The rule is, however, for a stone impacted in the common or hepatic ducts to produce long-lasting jaundice; and often, too, this follows when it is fixed in the cystic duct; the distension of this or the over-full gall bladder in these cases probably presses on the common duct. When the complete obstruction to the flow of bile has been in the common duct, this, the hepatic ducts, and those in the liver, are enormously dilated, and may contain a pint or two of fluid, and a distended duct has been mistaken for a distended gall bladder. If the cystic duct is completely obstructed, the gall bladder may be distended by its own colourless secretion, but more often it is empty and contracted. Even when a gallstone has been impacted for months, the symptoms may suddenly cease, because the stone has ulcerated into the intestine. It usually passes into the duodenum, the stone having been impacted in that part of the common duct which lies in the duodenal wall. If jaundice has been present, it then disappears; and the patient may get quite well, although she is, if the stone is very large, always liable to intestinal obstruction. Occasionally, the fistulous communication with the intestine allows bile, but not the gallstone, to pass into the gut. Death from cholæmia, due solely to the protracted jaundice caused by a calculus, is almost unknown. If the patient dies, it will be found that the calculus has set up carcinoma of the duct, or, in quite exceptional cases, ulceration and cicatricial constriction of it. It is of the greatest diagnostic importance to remember that protracted jaundice, due solely to a gallstone, rarely lasts more than three months. Deep jaundice of longer duration than this is almost invariably due to growth, and indeed jaundice of only three months is much more often due to this than to gallstones. The chief diagnostic points are the previous history, the other symptoms of growth, especially the irregular enlargement of the liver, and the fact that the obstruction to the flow of bile from a growth is more complete than from a stone, consequently fluctuations in the depth of the jaundice and in the colour of the usually pale stools are points in favour of gallstones, although slight fluctuations may be met with in growth.

Dilatation.—A distended gall bladder forms a pear-shaped and often painful tumour, usually situated just at the outer border of the right rectus, but sometimes nearer the nipple line, and sometimes more towards the middle line. It may reach to the umbilicus or even beyond it. It feels like a fluid tumour, it can be shifted laterally with the hand, and moves freely with respiration. The respiratory excursion of floating kidneys and omental tumours is usually much less, and can be prevented by putting the hand firmly on their upper part; but that of a gall bladder cannot, nor can this be felt bimanually as can a floating kidney. Distension of the stomach with gas renders a floating kidney very difficult to feel, but it simply pushes a distended gall bladder more to the right. The distended bladder is usually dull on percussion, but it must not be forgotten that if very distended it may become bent on itself, and then it sinks back into the abdomen, so that resonant colon or intestine

may come in front of it. Usually the diagnosis is so easy that an explor-
atory puncture is not needed, but if this method is adopted, a very fine short
sterilised needle must be used, and the tumour should be punctured where
dull and prominent. The fluid obtained has been secreted from the mucous
membrane of the gall bladder, and it is commonly free from bile, for this
soon gets reabsorbed after the obstruction is complete; it is usually clear,
contains little or no albumin, but mucin and pavement epithelium; but
if it is inflammatory, of course albumin and pus corpuscles are present.

After a gall bladder has been dilated some time, ridges of hypertrophied
muscle may be seen when it is opened, and later on the mucous membrane
atrophies, and may ulcerate where stones are in contact with it. These
ulcers may heal and cicatrise. In most cases the wall of the gall bladder
is finally much thickened. In some very rare cases it may be calcified, in
others septa form which may encapsule the calculi; and, lastly, the inner
surface of the gall bladder may become gangrenous. Distension of the
gall bladder is almost always due to impaction of a calculus in the
cystic duct, but exceptionally it may be caused by growth of the cystic
or common ducts, some pressure from without; or, still more rarely, the
gall bladder undergoes a paralytic distension, of which I have seen an
instance occurring in the course of typhoid fever.

Nearly always the course of events is that, secondary to obstruction of
the duct, an infective slight inflammation of the lining membrane of the
gall bladder is set up by the *Bacterium coli commune*, for this micro-organism
has been discovered in the fluid from distended gall bladders, which con-
tained but little albumin and only a few leucocytes, and which the older
observers would certainly not have called inflammatory, especially as often
there were no general signs, such as rigors, temperature, etc. But this is
not surprising when we remember that the virulence of this particular
micro-organism is very variable; but severe pyrexia, rigors, and sweating
may develop, and the number of leucocytes and the quantity of albumin
in the fluid may increase, until genuine pus is formed, and we have an
empyema of the gall bladder, in which case it is quite possible there may
be a secondary infection, with streptococci and staphylococci. But the
formation of pus is certainly rare; the usual course is for the fluid to
contain only a few leucocytes and a little albumin, and for the general
symptoms to be only moderately severe. As the cystic duct is commonly
blocked, the fluid cannot, by means of the bile ducts, infect the liver, and
consequently there are not usually abscesses there.

In some few cases, however, the fluid is absolutely sterile, and contains
no leucocytes or albumin, and the secretion of mucus in the gall bladder
may, in these cases, be compared to the collection of fluid in a hydrocele.
If it is sterile, or if it contains only a little albumin and a few leucocytes,
it may be completely absorbed, even when the obstruction persists; but if
the inflammation is more severe, it may, by spreading through the walls
of the gall bladder, set up acute peritonitis; or this structure may, when
its walls are softened, rupture into the peritoneal cavity, or externally
into some neighbouring viscus, when a fistula is formed. Gallstones may
be discharged through such fistulæ.

Abscess of the liver.—This is a rare result of a gallstone; neverthe-
less the following several varieties exist. The *B. coli communis* is always
present, and very often streptococci as well.

An empyema of the gall bladder may invade the liver. An abscess
around an impacted stone may form in the liver substance. A stone

may ulcerate through the wall of the duct in which it lies, into the liver, and form an abscess there. Suppuration may take place around one or more small calculi in the same branch, or in different branches of the hepatic duct; many of the smaller branches of the duct may thus become infected, so that at last the ducts are tubes of pus, and many minute abscesses may be present. According to some authorities, bile, dammed back in the smaller ducts, leads to necrosis of the liver cells, and suppuration takes place around these minute foci of dead cells. In very rare cases a stone in the common, cystic, or hepatic ducts may set up some local formation of pus, and the process may spread back along the ducts until the liver is riddled with tubes of pus and small abscesses connected with them. The most common form of hepatic abscess in association with gallstones is the following. An empyema of the gall bladder, or an abscess around a calculus, may directly infect a branch of the portal vein, and as a result, numerous small abscesses are found in the liver, just as in any other case of portal pyæmia. Inasmuch as the cystic vein is returned into the portal, metastatic venous abscesses in the liver may result from inflammation of the gall bladder and large bile ducts.

The recognition of abscess of the liver due to gallstone is often very difficult, for, as has already been pointed out, gallstones may, quite apart from any suppuration, cause rigors, pyrexia, and sweating, and a swollen, tender liver. Our guides must be that, if an abscess be present in the liver, the symptoms are more severe; the tenderness of the liver is more local, especially during the rigor, and if one abscess be large enough, there may be local signs, as swelling, extreme tenderness, etc.; but this often is not the case. If the severe signs persist some time, and the patient is dying, this is, of course, almost conclusive of hepatic suppuration; and signs of general infection, such as pulmonary abscesses, or malignant endocarditis, are absolutely conclusive. It may be quite impossible to distinguish between a suppurating growth and a hepatic abscess.

Fistulæ.—Gallstones may, either by ulceration or by rupture of an abscess around them, form fistulæ. The most common is a fistula into the duodenum, and this may be due either to a fistula between the gall bladder and this part of the intestine, or it may follow the impaction of a stone at the lower end of the common duct. The next most frequent is between the gall bladder and colon. A fistula through the anterior abdominal wall is rarer; it is usually at or near the umbilicus, and very rarely a fistula may form between the gall bladder and the stomach, the thorax, the jejunum, the ileum, the portal vein, or the urinary passages; and, lastly, a fistula may run into the retroperitoneal tissue, or lead to a communication between contiguous bile ducts. If the cystic duct is patent, and the gall bladder communicates with some viscus or the outer surface of the body, much bile may escape from the fistula; but often, with external fistulæ, the flow of bile is interfered with, as the passage is commonly tortuous; and therefore sometimes the patient is jaundiced, and she may die from cholæmia; but, apart from this, the presence of a permanent biliary fistula usually exhausts her so much that death results after a time. By far the least dangerous track is that which forms when a stone ulcerates from the duodenal end of the common duct into the duodenum. Often, when this has happened, the parts look so natural that care is necessary to demonstrate that ulceration has taken place. I once made a post-mortem examination on a case in which a fistulous communication existed between the gall bladder and pylorus. The surrounding inflammatory thickening led to constriction of

the pylorus, and the patient was thought, during life, to be suffering from malignant disease of the pylorus. As far as I know, every case on record in which, owing to a biliary fistula, a thickened pylorus existed, has, in the same way, been wrongly diagnosed. It should not be forgotten that the formation of a fistula may open a vessel and lead to considerable hæmorrhage.

Intestinal obstruction due to gallstone is treated of under the subject of intestinal obstruction generally. Here the only points which call for notice are, that often the ulceration of a stone from the gall bladder into the intestine is unaccompanied by either jaundice or pain, but nearly always a history of previous attacks of colic can be obtained; that obstruction is less likely if it passes straight into the colon than if it goes into the intestine, for the obstruction nearly always takes place a little above the ileo-cæcal valve. It is said to be a point in diagnosis that, although the obstruction appears otherwise complete, and fæcal vomiting may be present, yet flatus may be passed; but I am certain this is also true of growth, and as most of the patients are elderly, and the obstruction is chronic, having lasted usually rather over a week, the diagnosis commonly lies between growth and gallstone. In the last case under my care, as careful cross-questioning failed to reveal any history of colic, we regarded the case as one of growth; but a gallstone was found a little above the ileum, and, on subsequent inquiry, the patient's friends said she had misinformed us, as she had previously suffered from gallstones.

Biliary cirrhosis.—The teaching of Charcot and others has called wide attention to the view that obstruction to the flow of bile will set up cirrhosis of the liver, and that, consequently, the impaction of calculi will lead to cirrhosis. Ligature of the common duct will, in animals, cause a diffuse cirrhosis, and this may also sometimes be found, after death, in persons who have had biliary obstruction. When present, it is always of the hypertrophic variety. A further discussion on this subject will be found in the article on Cirrhosis of the Liver. We need only state here that biliary cirrhosis is never well enough marked to give rise to symptoms during life. It is a condition recognised in the post-mortem room, but not in the wards.

Carcinoma of the bile passages.—Hilton Fagge was the first in this country to point out that gallstones frequently lead to carcinoma, and Naunyn quotes 124 cases of carcinoma of the gall bladder, and in 114 gallstones were present. The growth may be either hard, soft, alveolar, or villous. From the cases I call to mind, the gall bladder is usually shrunken, and does not project from the under surface of the liver, although its walls are thickly infiltrated with growth; its cavity is much reduced, and contains gallstones and a little brown fluid. On the other hand, if the growth is chiefly confined to the neck, then the gall bladder distends and forms a large mass projecting from the under surface of the liver; and, in other rare cases, the growth itself may project as a tender mass from the under surface of the liver. Whether it has begun in the bladder, or in one of the ducts, it often spreads along these. Quite commonly, too, it extends by continuity into the hepatic substance, and it may grow into the colon; but I should certainly agree with the statement that genuine secondary metastatic growths in the liver are not as common in those cases in which the primary growth is in the gall bladder, as in those in which it is in some other organ at the periphery of the portal system. Owing to the frequency with which a gallstone is impacted at the duodenal portion of

the common duct, that is a common seat of growth, and it is quite possible that some growths, thought to be primary, in the head of the pancreas, really originate here. Whatever may be the primary seat, the glands in the transverse fissure may be enlarged, and if they press upon the common duct and portal vein, then jaundice and ascites may follow. Lastly, in some cases the peritoneum may become infected.[1]

Diagnosis.—There is no condition which is especially often confused with gallstone colic, but in some cases care will have to be exercised to distinguish it from the other painful abdominal diseases. The jaundice from the so-called catarrhal jaundice, does not usually subside so quickly as does that due to gallstones.

Treatment.—During an attack of gallstone colic, morphine should be injected subcutaneously till the pain is eased. Many like to use a mixture of morphine with a little atropin. Hot fomentations should be frequently applied over the region of the gall bladder, and the patient may be given plenty of hot water to drink; for although she will, because of the vomiting, quickly return it, after this has happened several times it is usually retained, and she is not more sick with the hot water than she would be without it. Great relief, too, is said to follow when hot water is thrown high up into the large bowel in considerable quantities. If the pain is very severe, the patient may inhale about as much chloroform as is used to relieve the pains of labour. Some advise a dose of 30 or 40 grs. of salicylate of sodium, but it is hardly likely that it will be retained.

Between the attacks, our object is to hurry the flow of bile, in order to prevent the formation of fresh calculi, and to move on any that may be present. For this purpose, the movements of the lower part of the thorax should be free, and no stays or other tight clothing should be worn; the patient should take plenty of outdoor exercise, of which riding and hill-climbing are perhaps the best forms; and as active, healthy digestion favours the flow of bile, the food should be restricted to a simple mixed diet, and it is important that enough food should be taken, and the patient should not go too long without it. But excess and improper food, as they lead to indigestion, should be especially avoided, and it appears that carbohydrates are not at all well digested. Active intestinal movements favour the flow of bile, and although the experimental evidence that most of the so-called cholagogues increase the biliary flow is slight, still, as these patients usually require aperients, drugs such as euonymin, calomel, powdered ipecacuanha, podophyllin or iridin, which are commonly classed as cholagogues, may be used; but clinical experience goes to show that the best aperient cholagogue for these patients is sulphate of sodium, from which it follows that it is excellent treatment to give at night a pill containing, say, 1 gr. of calomel, 1 of euonymin, and $\frac{1}{2}$ gr. of powdered ipecacuanha, followed, in the morning by such a quantity of a sulphate of sodium water—such as Friedrichshall, Æsculap, Pulna, or Hunyadi Janos— that, when mixed with half a tumbler of warm water and sipped during dressing, it will ensure that the bowels are well opened after breakfast. I have found a mixture of Æsculap and Hunyadi Janos very efficacious.

[1] Recent experience has shown that "simple infective cholangitis" is a sufficiently frequent complication of gallstones to merit description here. The chief symptoms are hepatic pain, jaundice, sometimes severe, but often slight and variable, an enlarged and tender liver, rigors, sweating, vomiting and pyrexia, lasting for many days or weeks without the formation of abscesses in the liver. Patients may for many years be subject to these attacks. Sometimes it is necessary to cut out the stone from the common duct, but often the patients recover without operative interference.

Salicylate of sodium favours the secretion of bile, and therefore 5 or 10 gr. of this should be taken thrice a day. It has already been mentioned that cholesterin is peculiarly soluble in olein, and Brockbank has shown that when a gallstone is placed in olive oil, and maintained at the temperature of the body, it loses 68 per cent. of its weight in ten days. Many observers, too, claim that distinct benefit follows the administration of large amounts of olive oil. I certainly have seen patients improve while taking it. Probably the administration of olive oil leads to the excretion of some of its olein in the bile, but experimental evidence on this point is wanting. Some patients will not take it at all, others take it neat. A little lemon-juice often makes it palatable, or it may be given with salad, or mashed up with either fish or potatoes. The patient should try to take at least 5 oz. a day, and may take 8 or 10. If she cannot take much of the oil, she may eat plenty of butter and fat, and use cream in her tea. Firm abdominal massage in the hepatic region is often useful, and if ordinary exercise cannot be obtained, gymnastics may be substituted.[1]

There is no doubt that sufferers from gallstone colic derive great benefit from going to places where hot sulphate and carbonate of sodium springs exist. As the patients, in addition to being given the water, are carefully dieted and take exercise, it is quite in accord with what has been said that they should do well. Carlsbad is by far the most popular resort, and many patients derive very great benefit from a visit there. It is usual to go in the summer. The waters contain sulphate, bicarbonate, and chloride of sodium, and their temperature as they leave the springs is between 122° and 158° F. Many patients go to Vichy (temperature of water, 112° F.), Ems (114° F.), and Neuenahr (95° F.). All these waters contain bicarbonate of sodium. Royat has similar warm springs. The waters of Marienbad and Leamington both contain much sulphate of sodium, but they are not hot.

If there is an empyema of the gall bladder, or an abscess around it, the treatment is the same as for an abscess of the liver (q.v.). If, either by rupture or spread of inflammation, acute peritonitis has been set up, the peritoneum should be thoroughly cleansed. If the patient has suffered from repeated attacks of biliary colic, which are wearing out his strength, and have not yielded to medical treatment, or if he has persistent jaundice from obstruction of the common duct, or if the gall bladder is so distended that it forms a painful tumour, which may rupture, the question of surgical interference should be carefully considered. Either the obstruction may be removed, or a communication may be established between the gall bladder and some part of the intestine. Stones from the gall bladder are easily evacuated when it is opened (cholecystotomy). This is best done by an incision in the right semilunar line, beginning at the costal margin. If there is no reason for hurry, the gall bladder may be stitched to the margins of the wound in the abdominal wall before it is opened, and whenever it is opened the wound should be carefully packed to prevent any extravasation of bile into the peritoneal cavity. Stones in the cystic duct may, after the gall bladder is opened, be extracted by forceps or scoop, and if they are very firmly fixed it may be necessary to first crush them. If the obstruction has been removed, bile will pass the natural way, and the opening in the gall bladder will close up. When the stone is in the common duct, the case is more difficult to manage. The

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[1] Eunahol, which is pure oleate of sodium, has been given in doses of 30 or 40 grs. without success.

duct may be incised, the stone turned out, and the wound in the duct stitched up again; or it may be crushed between the finger and thumb or with padded forceps, or it may be broken by a needle, and the pieces left to discharge into the duodenum. When the obstruction cannot be removed, the gall bladder may be made to communicate with the intestine (cholecyst-enterostomy). The directions given by Treves are as follow :—The abdomen is opened in the right semilunar line, and the gall bladder is exposed. The nearest loop of the upper jejunum is now brought up, and is fixed to the gall bladder by a row of sutures, arranged in a circle, and enclosing an area, if possible, equal to the lumen of the bowel. The gall bladder is now opened and emptied, and through this opening a communication is made between the gall bladder and the bowel within the area embraced by the suture line. If necessary, a few additional sutures are inserted. Then the opening in the gall bladder and that in the abdominal wall are closed. The operation may be done in stages—(1) The unopened gall bladder and unopened bowel are united by sutures ; (2) the gall bladder is opened, and then an incision is made from it into the bowel; (3) the incision into the gall bladder is closed. Murphy's button is often used in this operation. It may be necessary to excise the gall bladder (cholecystectomy). Mayo Robson says this may be done when, after cholecystotomy, the gall bladder is so contracted or softened that it cannot be sutured, and the common duct is patent, or when the cystic duct is completely obliterated. None of these operations should be undertaken lightly. They are often very difficult

ACTIVE HYPERÆMIA OF THE LIVER.

Venous distension of the liver, secondary to disease of the heart and lungs, will be described later ; but the quantity of blood in the liver may be increased in other ways. For instance, after each meal the organ is engorged, and it is quite likely that the dyspepsia which occurs in those who eat and drink too much may be associated with, and increased by, a lasting over-distension of the hepatic vessels, and this may be the cause of the sense of fulness and distension in the hepatic region of which these persons complain. They usually suffer from nausea, loss of appetite, a furred tongue, headache, constipation, and often an unusual drowsiness. A more limited and simple diet and a cholagogue purge generally benefit them ; and, to prevent further attacks, they should lead an active life, with plenty of exercise, and should be moderate and simple in their eating and drinking. From time to time they will require a purgative, and that combination already recommended for patients suffering from gallstones will be found most suitable.

Those who practise in tropical climates, especially India, are familiar with a much more severe form of congestion of the liver, which occurs among Europeans living in these climates. This condition is usually ascribed to the excessive heat, together with over-indulgence in alcohol and food. At first the patient often has a little diarrhœa, his liver is enlarged and tender, and there is considerable pain and heaviness under the right ribs ; he is slightly jaundiced, but as the months go on he becomes anæmic and sallow; he suffers from constipation, with pale motions ; his digestion is poor, and the enlargement of the liver becomes permanent. Men suffer much more than women, probably because they eat and drink more. Of

late years the number of persons in India suffering from diseases of the liver has been diminishing, probably because less alcohol is drunk than formerly. If an opportunity occurs at the early stage of this disease of seeing the liver, it is found to be intensely congested; later, it is harder and denser than in health. It may be necessary for these patients to give up living in tropical climates. They must always be very careful and moderate in the matter of eating and drinking, and the bowels should be kept carefully open.

DISEASES OF THE PORTAL VEIN.

The most important affection of the portal vein is thrombosis. Its most common causes are the extension into the vein of a nodule of malignant disease, growing either in the liver, pancreas, or glands in the transverse fissure, and cirrhosis of the liver. Occasionally the condition seems associated with perihepatitis, and sometimes there is nothing to suggest a cause. The clot may occupy the whole or only a part of the calibre of the vein, and in cirrhosis the patient may live long enough for the clot to completely organise, and then to shrink so that the walls of the portal vein come in contact with one another. The vein is replaced by an impervious narrow cord, and we have then the condition known as pylephlebitis adhesiva. This is excessively rare; it may be associated with frequently recurring ascites, but this is by no means always the case. No doubt, when, as usual, portal thrombosis extends up to the liver, the circulation is chiefly carried on by anastomosis between the portal and general venous systems; the mesenteric and splenic veins are much enlarged in one of our museum specimens. In dogs, when a ligature is applied to the portal vein, there is dilatation of the anastomosis between the branches of the portal vein, which enter it above and below the ligature, very little ascites develops, and the animal seems none the worse for the ligature. Considering the large size of the portal vein, and the sudden obstruction of a ligature, the absence of ascites can hardly be explained by the anastomosis. There is a specimen in the Guy's Museum, in which an aneurysm of the portal vein is associated with thrombosis of it. Thrombosis of the portal vein is, except in the very rare pylephlebitis adhesiva, of little clinical interest, and, indeed, we are first made aware of it at a post-mortem examination; but it may be associated with hæmatemesis. Suppurative pylephlebitis will be described in speaking of pyæmia.

DISEASES OF THE HEPATIC ARTERY.

Aneurysms of this artery are very rare. The symptoms which have been noted are pain, jaundice, and a tumour. A patient under my care had an aneurysm of each hepatic artery; the only symptom which could be set down to them was jaundice. These aneurysms usually rupture into the peritoneal cavity, but they may burst into the bile passages. Usually they are infective.

ABSCESS OF THE LIVER.

For clinical purposes these are best divided into two groups—multiple small abscesses, and solitary—in rare cases two or even three may be present at the same time—large abscesses.

MULTIPLE SMALL ABSCESSES.

These are always pyæmic, and usually the source of infection is at the periphery of the portal vein. Thus they are found after ulcer of the stomach, ulceration of the intestine and fistula, operations for piles, suppuration, or ulceration of the biliary channels, abscesses in the spleen, disease of the pancreas, appendicitis, and diseases of the female pelvic organs. In rare cases, multiple pyæmic abscesses are found in the liver as a result of general pyæmia.

Morbid anatomy and pathology.—When infection of the liver takes place through the portal vein, infective emboli are taken by it to the liver, and block the minute twigs of the portal vein, the liver becomes studded with small patches of necrotic tissue, and very quickly numbers of abscesses form; they are usually about the size of peas, but they may, however, be as large as a Tangerine orange. No gangrene of the liver is ever observed, and the patient almost always dies before an abscess ruptures into the peritoneal cavity or an adjacent viscus, but contiguous abscesses may run one into the other, and pus may be found in the hepatic veins. It is common, too, in cases of portal pyæmia, to find pus in the portal vein, and there is often also an acute phlebitis of it, together with much attached ante-mortem clot, and this condition is called acute pylephlebitis. In very rare instances, in which the infective material is only slightly toxic, pylephlebitis may, like acute inflammation of other veins, recover; then, as in other veins, the vessel becomes permanently occluded and even converted into a fibrous cord; this condition is called pylephlebitis adhesiva (see " Thrombosis "). It is highly improbable that there are any abscesses in the liver in those cases which recover. In a few instances of multiple pyæmic abscesses of the liver, the source of infection is at the distal end of some branches of the general venous system. This is difficult to understand, for before the infective emboli can reach the liver they must traverse the lungs, and it is not easy to explain why they should be able to pass the lungs and yet be arrested in the liver; it will not do to suppose that the liver is infected, from abscesses in the lungs set up by the original infection, for, according to Wilks and Moxon, the abscesses in the liver may appear older than those in the lungs; even in cases in which the infection might be expected to come from the lungs or the left side of the heart, pyæmic abscesses of the liver are very rare, for, owing to the free anastomosis between the portal and hepatic capillaries, it is very difficult to produce infarction of the hepatic artery.

Symptoms.—Although we can usually, from the presence of rigors, sweating, and the other signs of pyæmia, make out that the patient is suffering from this disease, yet there are hardly ever any local signs indicating that the liver is affected with multiple pyæmic abscesses.

Prognosis and treatment.—It need hardly be added that the prognosis of multiple pyæmic abscesses of the liver is very bad, and that no local treatment for the hepatic condition is possible.

SINGLE LARGE ABSCESSES.

These, which are almost always single, and never numerous, naturally fall into certain groups which may best be considered from an etiological standpoint.

Etiology.—The tropical abscess is often, but by no means always, associated with dysentery (tropical abscesses of the liver are found in about 20 per cent. of the cases of dysentery, and Kelsch and Kiener state that dysentery occurs in 75 per cent. of cases of tropical hepatic abscess), so that they have been said to be pyæmic, and due to absorption from dysenteric ulcers. This is incorrect, for we have seen that the ordinary pyæmic abscess of the liver is multiple and small, not solitary and large; and further, in many cases of dysentery, typical pyæmic abscesses of the liver are found—presumably due to pyæmic infection through the dysenteric ulcers—and these may even be associated in the same liver with the large tropical abscess. Then the amœba, which many observers believe to be the cause of dysentery (*q.v.*), has been found in the pus of these large hepatic abscesses; and it is quite possible that when the large hepatic abscess is unassociated with dysentery, that the dysenteric amœba has gained entrance into the portal vein without causing dysenteric ulcers in the intestine, just as the scolices of the *Tænia echinococcus* may gain an entrance into this vein without exciting any reaction at the point of entrance. If it is urged that, on this view, it is strange that tropical abscesses should usually be solitary, and never exceed one or two, we must remember that usually there is only one hydatid in the liver. But although for the above reasons, derived from morbid anatomy, there is no doubt that the large abscess is not pyæmic, and is frequently associated with dysentery, yet the bacteriology of the subject is far from complete, for authors are not yet unanimous that the amœba coli is the cause of dysentery; some have failed to find it in the pus of tropical abscess, although they have found many other organisms, as streptococci, staphylococci, and *B. coli*, while others again have reported that the pus is sterile, but this statement does not exclude the amœba. The frequency of tropical abscess is lessening. This is attributed to better sanitation and less indulgence in large meals and alcohol. In English practice these abscesses are usually found in those who have resided in the tropical parts of India and the East Indies, but they also occur in persons coming from other tropical regions, as the Southern States of America.

Large abscesses closely resembling tropical abscesses may in rare instances occur in those who have never left England. Sometimes these are associated with ulcerative colitis, as in a case I recorded in 1894, and other cases are given by Fagge and Dickinson. Such cases certainly suggest that there is some special micro-organism responsible for the ulcerative colitis, which, being taken up by the portal vein, causes the hepatic abscess. A hydatid may suppurate, and thus be the cause of a hepatic abscess. A blow in the hepatic region may cause an abscess in the liver, but it sometimes leads to an abscess between the liver and diaphragm. Suppuration may occur around foreign bodies embedded in the liver; thus a round worm has been found in the centre of an abscess. In very rare instances a hepatic abscess is due to the spreading into the liver of some neighbouring suppuration. Suppuration of the gall bladder, suppuration around a gallstone, and suppuration of the bile ducts (suppur-

ating cholangitis) leading to abscesses in the liver have been described under the head of Gallstones. Occasionally we meet with suppuration of the gall bladder which is independent of gallstones.

Morbid anatomy.—The whole liver is usually enlarged, congested, and a little soft. The abscess may contain several pints of pus, and I have seen it so large that the hepatic tissue was a mere shell. Its cavity is irregular, and has ragged walls with shreds of dead liver tissue attached to it; the liver tissue immediately around it is hyperæmic and soft, although, if the abscess has lasted some time, it may have a thick well-defined capsule; the pus is often of an anchovy paste colour, due to the admixture with it of disintegrated hepatic tissue. A suppurating hydatid is shut off by its capsule from the surrounding hepatic tissue; therefore its limits are always sharply marked, and the pus is always yellow. If the abscess is opened or discharges naturally, it may heal, leaving a cicatrised scar in the liver.

Symptoms.—Occasionally hepatic abscesses are found in the post-mortem room, when there were no indications during life of their presence, but usually the first symptoms are those of fever; the temperature is raised, the pulse quickened, and the patient feels out of sorts. It is important to notice that throughout the whole course of the disease the temperature chart is often very like one belonging to a patient suffering from ague, for the temperature may rise to 104° or more, and suddenly fall to normal, with equal periods between each rise; sweating, too, may be very marked; and mistakes between ague and hepatic abscess are by no means rare, for signs specially pointing to the liver are often absent when the abscess is small and deep-seated. But in most cases the liver sooner or later enlarges, and as the abscess approaches the surface, the enlargement becomes irregular and the shape of the organ is distorted. As it is, most often at the upper and back part of the right lobe we get a dome-shaped increase of the hepatic dulness in the axillary or scapular line, with perhaps later on some bulging of the right lower ribs and signs of compression of the lung. The lower edge of the organ is pushed down and can be felt easily below the ribs, and if the abscess is mostly on the front of the right lobe, we may feel a lower prominence through the abdominal wall, and the lower edge of the liver becomes further removed from the abdominal wall, and intestine may come in front of it, and then a mistake as to the size of the organ is very easy. When the abscess is quite close to the lower edge, this of course becomes very rounded. If there is actual bulging, the prominence is tense, rounded, smooth, free from any inequalities, and fluctuation may sometimes be detected. Pain and tenderness are often absent. If the pain is acute and tearing, it indicates that the abscess is near the surface, and perihepatitis has supervened; but if the pain is dull and heavy, the pus is deep in the organ. Occasionally there is pain in the right shoulder, and there may be a hacking reflex cough; jaundice, ascites, œdema of the lower extremities, distension of the superficial veins of the abdomen, and enlargement of the spleen, are not distinguishing features of hepatic abscess, and are rare in the course of it, and when present are accidental complications due to pressure of the abscess. Vomiting is not uncommon; the urine is high coloured and loaded with lithates; albuminuria, if present, is usually febrile. Right pleurisy is not a rare complication. An abscess of the liver may exist many months, the patient then becomes extremely weak and wasted, and passes into the hectic condition, and finally dies exhausted; but if untreated, the abscess may burst into the right pleura or

into the right lung; it may discharge externally into the peritoneal cavity, the stomach, the duodenum, the transverse colon, or the biliary passages. In much rarer cases it has been known to open into the pericardium, the portal vein, the vena cava, or the pelvis of the kidney. Occasionally it causes serious hæmorrhage, because it lays open some large blood vessel. Of these complications the bursting into the right pleura and right lung are most common. Both are usually preceded by a particularly distressing cough, and when discharge takes place into the lung the pus coughed up is brick-red in colour, and there are physical signs of consolidation of the lung. The patient may recover from this condition, but he often dies from exhaustion.

Diagnosis.—The difficulty of diagnosis from ague has been mentioned. The examination of the blood will help us, for in suppuration we shall notice the increased leucocytosis, and in ague the *Plasmodium malariæ.* An empyema can usually be distinguished by noticing that the upper limit of the dulness is horizontal, but an encysted right-sided empyema may give rise to great difficulty. It is, however, very rare. Still more difficult is the distinction between a hepatic abscess and one between the diaphragm and liver. Here history of residence in the tropics will be a great help, and the pus withdrawn may be of an anchovy paste colour and contain dysenteric amœbæ; and these facts also aid us in distinguishing between an abscess of the liver and a suppurating hydatid. Pyæmic abscesses of the liver are never large enough to cause local signs, but a deep-seated non-pyæmic abscess may give rise to none. The history will then be our best help. Lastly, an abscess of the liver may be easily confounded with the intermittent pyrexia which is associated with gall-stones.

Prognosis.—Unless the abscess is opened artificially, this is very bad; at least 80 per cent. of the cases which are not operated upon die, those that recover mostly discharge through the lung. Even when the abscess is opened, the patient often dies from exhaustion, for he may not present himself for treatment until it is already of a large size.

Treatment.—If an abscess of the liver is suspected, a long exploring needle should be thrust into the organ at the point at which it is thought the pus comes nearest to the surface, and this operation may be repeated two or three times if the first exploration fails to discover pus. When the pus has been found, the case becomes surgical rather than medical, for it must be evacuated as soon as possible. If the abscess is near the surface of the liver, this organ is probably adherent to the abdominal wall, in the position chosen for evacuation; if it is not, the liver may be stitched to the abdominal wall; and if the wound is carefully packed, the abscess may, if the case is urgent, be opened at once; but as the escape of pus into the peritoneal cavity would be an extremely grave complication, it is better if possible to wait a few days till adhesions have formed and then to open the abscess. When the abscess has been opened, any septa in it should be broken down and a very wide drainage tube inserted. If the abscess is at the back, the attempt must be made to open it without wounding the pleura and peritoneum; if this is impossible, it may be necessary to drain the abscess through the pleural cavity. The patient should be well fed, and treated on general principles.

CIRRHOSIS OF THE LIVER.

If a student were to derive his knowledge of cirrhosis of the liver from the wards and post-mortem room, he would soon gain an accurate conception of the disease; but if he were to try to learn solely from books, it is probable that the more he read the more confused he would become. I shall therefore first give a description of the disease as usually seen, and then the reader will be in a better position to understand the controversial points.

ALCOHOLIC CIRRHOSIS.

This forms one of the commonest hepatic affections of temperate climates.

Etiology.—Although a number of causes, as backward pressure from heart disease, that will be mentioned later, may induce some cirrhosis, yet we know of no cause operative in this country, other than alcohol, which will produce such a degree of cirrhosis that it will either give rise to symptoms, or after death alter the liver to such a degree that this will be easily recognised, on macroscopical examination, as considerably cirrhotic. No doubt sometimes (especially in children) no history of alcohol can be obtained, but then none of the other factors which have been erroneously supposed to cause well-marked cirrhosis are present, and even in children a very careful inquiry will often show that alcohol was taken, when at first this is denied. We know nothing as to the causes of the few cases of well-marked cirrhosis not due to alcohol. Cirrhosis is most common between the ages of 30 and 60, and the sufferers from it are not often drunk, but take small quantities of alcohol constantly throughout the day. The disease is about equally common in men and women.

Morbid anatomy.—The chief determining causes of the alterations in the physical condition of the liver are the increase of fibrous tissue and fat, and the atrophy of the liver cells. The first makes the cirrhotic liver very hard and tough, so that it may even creak when cut with a knife. The new fibrous tissue may be easily visible to the naked eye; it is uniformly distributed throughout the liver, and never occurs as wide radiating bands, which are characteristic of syphilis. When it is around the lobules it is said to be perilobular; if areas composed of several lobules are formed by the fibrous tissue, it is multilobular; if each area contains one lobule, it is monolobular; and if individual lobules are invaded, it is intralobular cirrhosis. When the new fibrous tissue contracts, as in the kidney, so in the liver, the surface of the organ becomes granular; but frequently the contracting bands of fibrous tissue, being further apart than is the case in the kidney, the islets of projecting liver substance are larger, and in such cases the organ is commonly said to be hobnailed, and its edge is uneven. The new fibrous tissue is grey, and the islets of liver substance are varying shades of yellow and brown, according to the relative quantities of fat or bile pigment in them. On section, the same contrast of grey bands and yellow fatty islets is seen. The new-formed bands are, if young, made up chiefly of cells; if older, they are fully-developed fibrous tissue. They are supplied with blood from new-formed branches of the hepatic artery; but as they contract they slowly obliterate the minute branches of the portal vein, which are filled with clot, because of the retardation of the current in them; and occasionally the portal vein itself may contain an ante-mortem thrombus. The bile ducts withstand the pressure much longer; indeed, it is doubtful

whether the bile staining of the liver is due to compression of them. The pressure exerted on the islets of liver tissue is so considerable, that often when the liver is cut they at once rise and project on the surface of the section; slowly they may undergo complete atrophy, and neighbouring bands of fibrous tissue by their coalescence form wider bands. Most authors assume that the degeneration of the cells is secondary to the contraction of the fibrous tissue, but we must, as Mott points out, remember that the atrophy of the cells may occur before the fibrous tissue has begun to contract. It is clear that the size of a cirrhotic liver must be very variable, for the formation of embryonic tissue will at first increase it; but as this becomes fibrous and contracts, the liver will diminish in size, which diminution will become more marked as the atrophy of the liver cells sets in. Then, too, the amount of fat in a cirrhotic liver is of great importance in determining its size; all very large cirrhotic livers contain much fat. As a result of these varying factors, a cirrhotic liver may vary in weight between 2 and 9 lb. Price found that, out of 130 cases of fatal cirrhosis, in nine the liver weighed less than 40 oz., in twenty between 40 and 50, in thirty-three between 50 and 60, in thirty-one between 60 and 80, in twenty-five between 80 and 100, in ten between 100 and 150, and in two over 150. That is to say, twenty-nine livers were below the normal weight, thirty-three were of the normal weight, and seventy-eight were above it. The peritoneum over the liver is frequently thickened and opaque, and there are often adhesions to the abdominal wall; signs of general chronic peritonitis are too often seen, and so the mesentery is occasionally retracted, the peritoneum generally may be opaque, the intestines may be welded together into a lump, the gut may be shortened, and the wall of it and the stomach may be obviously thickened. The spleen and pancreas are usually hard, and the subjects of cirrhosis may have a fatty heart, atheromatous vessels, granular kidneys, or œdematous lungs.

The anastomoses between the portal and general venous systems are much dilated. By far the most important are those between the middle and inferior hæmorrhoidal, and between the gastric and œsophageal veins. Others exist between the capsular branches of the portal which supply the liver, and by means of its ligaments communicate with those of the diaphragm; between the portal branches which, running in the round and suspensory ligaments, reach the umbilicus and anastomose with the branches of the internal mammary and epigastric veins; between the portal branches in the intestinal walls, and branches going into the inferior cava.

Pathology.—It is erroneous to regard cirrhosis of the liver as a purely local disease of that organ. In many respects it reminds us of chronic interstitial nephritis. In both diseases we have a similar morbid anatomy, and many symptoms showing that the effects are felt far beyond the organ chiefly affected; in cirrhosis there are the sudden onset of ascites (apart from any sudden increase in portal obstruction), the frequent slight chronic peritonitis, the œdema of the feet, the nervous symptoms, the changes in the blood (of which the jaundice is possibly an expression), the liability to hæmorrhages, and the pyrexia. Of these, the ascites, the œdema of the feet, and the nervous symptoms are, like those of uræmia, liable to come on so suddenly that we can hardly help supposing that the cirrhotic liver or the cirrhotic kidney has suddenly failed to excrete, or has suddenly manufactured some poison, which is usually fatal, and kills probably by causing, in both cases, both respiratory and cardiac failure; in both diseases it appears extremely likely that the more

chronic symptoms are also toxic. Lastly, both cirrhosis of the liver or kidney, as the case may be, is often found after death when its presence was quite unsuspected during life. Experiments do not help us much to understand the disease, for well-marked cirrhosis cannot be produced by giving alcohol to animals. It only makes their liver fatty. This is interesting when we bear in mind that some sufferers from cirrhosis have not taken much alcohol.

Symptoms.—It is important to remember that cirrhosis is very frequently found post-mortem in persons who have during life shown no signs of it, and sometimes in these cases the liver is small, and this suggests that the disease has been present some time. Animals in whom the portal vein is led directly into the inferior vena cava, may live a long time, so that, when the liver is slowly destroyed by cirrhosis, it is not surprising that the patients may survive, especially as the destruction of liver tissue is never complete, and no symptoms need arise from the obliteration of minute branches of the portal vein if the collateral circulation is well maintained.

Physical examination.—If the liver is enlarged, this may often be made out both by percussion and palpation; and even if ascites is present, the liver may be felt by suddenly pressing down on it; the lower margin may be at the umbilicus, or lower; the surface can often be felt to be hard and hobnailed; and the lower edge, too, is hard and somewhat uneven. Sometimes, even when the organ is not enlarged, this characteristic edge may be felt, if the fingers be thrust well under the ribs and the patient inspires deeply. On the other hand, it is often impossible to feel the organ, and the hepatic dulness on the chest wall may be diminished. But owing to the presence of emphysema, the varying state of distension of the stomach and intestine, the resistance and thickness of the abdominal walls, the presence of ascitic fluid, the stretching of the hepatic ligaments, and tight-lacing, it is often impossible during life to accurately estimate the size of the liver, and still less its weight, for its specific gravity varies according to the amount of fat in it. As a rule, the organ is neither painful nor tender, but it may be if there is a little local peritonitis over it.

The patient often has the aspect of a drinker; his nose is red, the venules on his face are dilated, and his skin is of a muddy tint. He complains of loss of appetite, a nasty taste in his mouth, nausea and sickness, especially in the morning. The tongue is furred, the bowels are mostly constipated, but there may be attacks of diarrhœa. There is much flatulence; often, too, he is somewhat wasted. Many of these symptoms are no doubt directly due to the effect of the alcohol on the gastro-intestinal mucous membrane, but some may in part be the result of portal congestion, which very frequently causes piles and hæmatemesis. The bleeding may be very severe and the hæmatemesis may be fatal. Melæna may be present, even when the patient does not suffer from hæmatemesis or piles; and I have seen the whole of the stomach and intestines of that slaty colour which is so suggestive of old blood extravasation in their walls.

Ascites is a common symptom; it is more often associated with a small liver than a large, probably therefore pressure on the portal venules in the liver has something to do with it. But it is not due to this alone. Dr. Starling and I performed some experiments on dogs, and we found that the portal vein could be firmly ligatured without any ascites, and that it was much easier to produce ascites by damage to the peritoneum than by portal ligature; and in cases of malignant disease about the transverse fissure of the liver, there may be no ascites, even when the portal vein appears com-

pressed. On the other hand, as has already been mentioned, chronic peritonitis is often seen in association with cirrhosis; and as I have for some time past been accustomed to teach that this bears an important part in the production of the ascites, I am very pleased to see that Auscher, in his recently published article, says that peritoneal lesions are an undoubted cause of ascites in cirrhosis of the liver. The supervention of ascites augurs ill. Out of twenty-four cases of cirrhosis with ascites which I collected, in ten, in which the fluid was never enough to call for tapping, the average duration of life after the patient first noticed the abdomen to be enlarging was two months; and among the fourteen who needed tapping it was also two months; and in only two cases was life prolonged beyond three months.

Indeed, the onset of ascites usually means that the end is near, from which it follows that the patient hardly ever lives long after the abdomen is tapped; so true is this, that if the abdomen is tapped a second time, the case is almost certainly not one of uncomplicated cirrhosis, most probably the patient has chronic peritonitis. The fatal cases which die soon after tapping show the rate at which the fluid may be poured out, for I have known the abdomen, when the patient died, to contain 6 pints, although he was tapped five days before. The mere paracentesis is not the cause of the fatal result, for the abdomen may be tapped even hundreds of times in other conditions without any evil results. The fact that soon after the onset of ascites very many patients die—apparently from some auto-intoxication—suggests that, although the pressure on the portal vein and the state of the peritoneum are partly responsible for the ascites, yet it may in part be due to some poison acting upon the peritoneum as a lymphagogue. The ascitic fluid is of a pale straw colour, of a specific gravity of 1010 to 1016; it contains albumin and a trace of salts, but no blood. The feet are often swollen, especially about the ankles, and this is usually set down to pressure of either the enlarged liver or the ascitic fluid on the inferior vena cava; but this is not always the cause, for œdema of the feet may be present when the liver is not very large, when there is little or no fluid in the abdomen, and when no enlargement of the superficial abdominal veins can be noticed. Further, patients often say that they noticed the swelling of the feet at the same time as, or before, the abdominal distension. Probably it should, like the ascites, be regarded as evidence that there is general poisoning. The superficial veins of the abdomen are enlarged, if the venous communication at the umbilicus is well marked. Dyspnœa may be noticed, if the ascites is extreme.

Jaundice is rarely deep. It is commoner when the liver is large than when it is small, and, as the pressure on the bile ducts is less when the organ is large, probably we ought to regard the jaundice as chiefly due to pigment destruction in the blood, especially as there is never any evidence, such as dilatation of minute ducts, that the biliary channels were compressed. It is, as a rule, a bad sign, but cases are on record in which it has persisted for years. It appears that little bile is secreted, for the gall bladder is commonly empty, and the motions, although not so white as when the bile duct is completely obstructed, may be rather pale. A slow pulse, and other signs commonly associated with jaundice, are very rare.

Urine is high-coloured, rather scanty, and it contains much urobilin and lithates; if jaundice is present, there may be some bile. Often there is a little albumin, but the same persons who are liable to cirrhosis are those in whom we should expect to meet with a granular kidney; and if the ascites is extreme, the albuminuria may be due to pressure on the renal

veins. When the liver is enlarged, the quantity of urea excreted may be greater than normal; in the atrophic cases it is diminished, but the total amount of ammoniacal salts excreted is said by many observers to be increased. The spleen may be enlarged and easily felt. This is most frequent when the liver is enlarged, and is probably due to obstructed portal flow. Later on the spleen becomes small and hard. The temperature is usually normal, but it may be about 100° or 101° in the evening even if no complications are present. Hæmatemesis and melæna have already been mentioned; epistaxis and a mild degree of purpura may also be seen. The number of red corpuscles and the quantity of hæmoglobin are below normal.

The onset of nervous symptoms renders the outlook very grave, and if they are well marked the patient usually dies in a few days after their onset. Coma is the most frequent, but he may have convulsions, and be noisy, delirious, and so difficult to manage that it is necessary to place him in a strong room. These symptoms are almost certainly the result of auto-intoxication, but the poison causing them has not yet been isolated; it is not bile pigment, for although the patients who show these symptoms are often jaundiced, yet they bear no relationship to the depth of the jaundice, which is usually slight, and they may be present when there is no jaundice. Possibly the poison is derived from the failure of the diseased liver to form urea, for we know that urea is much less poisonous than its antecedents, and in acute yellow atrophy (which rapidly causes death) there is a failure to form urea. Then, too, carbamate of ammonia kills by nervous symptoms when the liver is thrown out of the circulation, by directly connecting the portal vein with the vena cava, but not otherwise, and it is a product of nitrogenous metabolism, and is probably converted into urea.

Any of the other effects of over-indulgence in alcohol, such as peripheral neuritis, may be coincident with cirrhosis, but often the whole brunt falls upon the liver. Alcoholic subjects are particularly prone to phthisis, often they show a considerable degree of atheroma, and granular kidneys and gout may be present. They often have œdema of the bases of their lungs, and pleural effusion, usually right-sided, is by no means rare.

Prognosis.—The chief points about this have been indicated. If the symptoms are slight, the patient may, with care, live a long time. Ascites and nerve symptoms are especially bad, but I have known cases, in which a considerable amount of fluid was present, lose all symptoms under treatment. The commonest cause of death is auto-intoxication, but hæmatemesis, melæna, and tuberculosis, especially of the lungs and peritoneum, are not infrequent.

Treatment.—It is, of course, essential that the patient should give up alcoholic drinks. His diet should be very simple; indeed, some authors advise milk, but this will probably lead to distaste for it, so that fish or white meat, bread and butter, toast, plain vegetables, and farinaceous puddings should form the chief articles of food. It is usually necessary, either on account of the constipation or the piles, to order an aperient to be taken two or three times a week, and these patients do very well on some sulphate of soda or magnesia water, as Æsculap, Friedrichshall, or Pullna, on rising in the morning, and a pill, containing a little calomel, ipecacuanha, or euonymin, in the evening. A mixture containing some nux vomica and dilute nitrohydrochloric acid is of service in restoring the flagging appetite. Three weeks at Carlsbad frequently does much good. If ascites

is present, I know of no drug better than copaiba resina; it acts as a diuretic, and, as I have often seen, a large amount of fluid may disappear entirely under its use. Fifteen gr. of copaiba resina, suspended with some compound tragacanth powder, and flavoured with some spirits of chloroform, taken four times a day, form a suitable dose. Paracentesis should only be done when the dyspnœa it causes is serious. The mere removal of the fluid is of no benefit to any of the other symptoms. Lately the omentum has been stitched to the abdominal wall, in order to help the formation of anastomosis between the general and portal venous systems, but we have not yet sufficient experience of this operation. I know of one case in which the patient was in no way benefited by it.

HYPERTROPHIC CIRRHOSIS.

In France it is believed that there is a distinct disease, not specially related to alcohol, and in which the liver is enlarged, ascites rare, jaundice common, and splenic enlargement frequent. The liver is always very much enlarged and hard, but not hobnailed; the jaundice is well marked and lasting; slight pyrexia is common; the urine contains bile, no albumin, no excess of lithates, and a diminished quantity of urea. The pulse is not slowed, there is marked leucocytosis. The patient is liable to crises in which there is hepatic pain, and all the symptoms become worse, but the disease often lasts some years. It occurs at a younger age than ordinary cirrhosis, and is commoner in men than women. A special form is described in children, in whom the spleen may reach to the pelvis, and the patients may be observed to have some enlargement of the fingers and toes. Many observers, however, do not draw any distinction between hypertrophic cirrhosis and ordinary cirrhosis; they urge that the intermediate cases are very common, that many patients with hypertrophic cirrhosis have taken alcohol, and that in genuine alcoholic cirrhosis the liver is often enlarged, and that the so-called hypertrophic cirrhosis may be the early stage of a cirrhosis that will later contract up. The chief of those who regard hypertrophic cirrhosis, or "La cirrhose hypertrophique avec ictere chronique," or "La cirrhose de Hanot" (who gave a very full description of it), as a separate disease, belong to the French school. They regard its cause as unknown, and point out that many of the patients have not taken alcohol to excess, that in many points (character of liver, frequent persistent jaundice, enlarged spleen, absence of ascites, and age) the disease differs from ordinary cirrhosis. Moreover, they believe that this disease corresponds to the cirrhosis that may be induced by ligature of the bile ducts, and that it is perilobular and intralobular, while ordinary cirrhosis is a venous and not a bile duct cirrhosis, and it is multilobular and extralobular. For my own part, I do not think that in London the distinction between the two forms is very marked, but I have seen a case which appeared to be an example of the special variety which occurs in children.

MALARIAL CIRRHOSIS.

Persons who have been in the tropics, and who have had frequent attacks of ague, often have an enlarged liver, which remains large for many years after their removal from the district infested with ague. I have seen the organ reach down to the umbilicus; it feels hard, and its surface is uniform. The spleen, too, is much increased in size. Although these patients may

be a little jaundiced, generally they only show the pale, sallow tint so common in those who have had ague. When the more usual signs of cirrhosis are present, it is usually difficult to be sure that alcohol may not have been at least a partial cause of the cirrhosis. The increase of fibrous tissue is seen chiefly in the portal canals, and often there is much brown pigmentation.

SATURNINE CIRRHOSIS.

A few cases have been put on record, in which lead was thought to induce atrophic cirrhosis; and we must remember that lead will cause cirrhosis of the kidney, and that it is very largely stored in the liver. If, however, saturnine hepatic cirrhosis exists, it is excessively rare.

OTHER FORMS OF CIRRHOSIS.

Dyspeptic cirrhosis has been described, and, no doubt, excess of food will lead to congestion of the liver; and it is conceivable that this might go on to cirrhosis, but the excess of food is so frequently associated with over-indulgence in alcohol, that it is impossible to separate the two conditions, and for the same reason it is difficult to be sure if there is such a disease as gouty cirrhosis. A diabetic cirrhosis, too, has been described, but probably on insufficient grounds. The long-standing congestion of heart disease, although it increases the fibrous tissue of the liver, does not lead to anything which ought to be confounded, during life or after death, with alcoholic cirrhosis.

An increase in the fibrous tissue of the liver occurs in animals, when the bile ducts are ligatured; and some cases have been described as calculus cirrhosis, in which it has been thought that obstruction from a gallstone may have been the cause of the cirrhosis, but when we remember that this form of cirrhosis is admittedly very rare, although gallstones are common, it becomes by no means certain that we have, in medicine, anything to correspond to experimental biliary cirrhosis.

A tuberculous and a syphilitic cirrhosis have been described, but these ought not, either during life or after death, to be confounded with alcoholic cirrhosis.

Much confusion has been caused by using the term cirrhosis to express the slight increase of leucocytes and vascular dilatation sometimes seen in the liver after specific fevers, *e.g.* smallpox. These changes are not visible to the naked eye, and give rise to none of the symptoms of cirrhosis.

I trust that I have now made it clear that, although, to the confusion of the reader, many forms of cirrhosis besides that which we in England commonly see, have been described, they none of them produce the symptoms or the alteration in the liver which constitute the disease to which we in England commonly give the name, cirrhosis of the liver.

NEW FORMATIONS IN THE LIVER.

MALIGNANT DISEASE OF THE LIVER.

This may be either cancerous or sarcomatous, and either form of growth may be either primary or secondary. Secondary cancer is so much the commoner that it will be better to describe it first.

SECONDARY CANCER OF THE LIVER.

This is a common disease. Thus at Guy's Hospital, during the years 1888–1893, both inclusive, at least fifty-three patients were considered during life to be suffering from secondary cancer of the liver, and during the same period there were fifteen cases of hepatic syphilis, twelve of abscess, twelve of hydatid, and seven of sarcoma of the liver. But it is really commoner, because often small secondary deposits are unsuspected during life; for, during the same period, 126 examples of secondary carcinomatous deposits in the liver were met with out of 4200 post-mortem examinations, and 50 per cent. of all persons in whom, at death, malignant disease of any organ is found, have secondary deposits in the liver.

Etiology.—The primary seat is usually found in the periphery of the portal system, but it may be in any organ which can· be affected with primary cancer. The stomach is the seat in more than a quarter of all the cases. The gall bladder, especially when it has been irritated by gall-stones, the pancreas, especially its head, and the rectum, are all common primary seats. The greater frequency of cancer of the pelvic organs and breasts of women explains the fact; the proportion of males to females who have cancer in the liver, is 3 to 4.

Morbid anatomy.—If the patient die soon after the infection of the liver, only a few small scattered nodules are seen; but as the primary seat is usually at the periphery of the portal vein, the liver often becomes affected early, and therefore, at death, large masses of growth are found in it, and it is very heavy; it may weigh as much as 20 lbs. The masses are scattered very irregularly throughout it, but it is rare to find any inside, unless they are visible on the surface. They may be microscopic in size, or they may be as large as a foetal head, and in a marked case the liver has large bosses all over it. The nodules are at first globular, but from irregular growth and because those which are contiguous coalesce, they soon become of all shapes and sizes. On section, these sharply defined masses stand out in strong contrast against the liver substance, which may be altered in colour by bile staining, hæmorrhage, or fatty degeneration, and which is gradually destroyed by the growth. The nodules vary somewhat in colour and consistency, for they reproduce exactly the characters of the primary disease. They are supplied with blood by branches of the hepatic artery, which run along their fibrous septa. ·After a time their centre degenerates, softens, and is absorbed; and the fibrous tissue contracts, so that if a nodule is on the surface of the liver, it becomes umbilicated. The degeneration may lead to a collection of fluid in the centre of the growth, or a vessel may be laid open, and then considerable hæmorrhage takes place.

The growth may appear to spread to the gall bladder and stomach, but in such a case these organs are nearly always the primary seat, and the disease has spread from them to the liver. As already mentioned, the glands on the transverse fissure are very frequently enlarged, the cancer often spreads along the obliterated umbilical vein, and a nodule may be felt at the umbilicus; the diaphragm and parietal peritoneum, too, are often implicated, especially where they are in contact with the liver. If the common duct is compressed, all the ducts and the gall bladder are very dilated, but if the cystic duct is compressed, the gall bladder is usually contracted, and contains only a little mucus. It is rare for the growth to spread to the suprarenal capsule, duodenum, or colon.

Symptoms.—If the case is one in which, during life, the diagnosis of cancer of the liver can be made, it is usually, both by percussion and tactile examination, discovered to be enlarged. It may reach below the umbilicus, up to the fifth rib in the midaxillary line, and out as far as the spleen. It moves up and down with respiration; this movement may be visible, and the lower ribs may be bulged outwards. The edge and surface are hard; and if carcinomatous nodules are felt, the organ is irregular and knobby, and the nodules may be even made out to be umbilicated, and this is diagnostic of cancer. Occasionally a rub, due either to local peritonitis or the friction of a parietal against a hepatic nodule, may be heard. The cancer may grow so fast, that an increase in the hepatic enlargement can be made out in the course of a week; if an increase can be detected within a day, it indicates hæmorrhage into the growth. The umbilicus may be the seat of a carcinomatous deposit, and then it is enlarged and hard. Pain and tenderness over the liver are often met with, but not infrequently they are absent; pain in the right shoulder is very characteristic. If the liver is hard, the sense of dragging may be very distressing.

About half the patients suffering from carcinoma of the liver are jaundiced, and this is due to implication of the glands in the transverse fissure of the liver, which, being enlarged, press upon the common duct. By far the most frequent cause of long-standing jaundice is carcinoma of the liver; in fact, it is almost the only cause in elderly people. The jaundice gradually becomes deeper and darker, and at last it is a deep olive hue. The gall bladder is often distended, and all the symptoms described under the heading of jaundice, as due to the presence of bile in the blood, are often seen, and then the patient usually becomes more and more drowsy, with, in rare cases, an occasional convulsion; the coma slowly deepens, and often, for several days before the end, it would be difficult for a superficial observer to say if the patient is alive or dead.

Ascites is rather less frequent than jaundice, and the two are associated in about 20 per cent. of all cases of cancer of the liver, diagnosed as such during life. The ascitic fluid is clear, often bile stained, and it may contain blood. The pressure of the enlarged glands in the transverse fissure is, no doubt, in part a cause for the collection of fluid in the abdomen, but it is doubtful whether it is the sole cause; for the size of the glands bears little relation to the amount of ascitic fluid, and the portal vein can be ligatured in dogs, and yet no ascites follows. On the other hand, in cancer of the liver, some part of the peritoneum is usually affected by growth, so it may well be that the fluid is due more to a cancerous peritonitis than to pressure on the portal vein.

A very large liver may hamper the movements of the right side of the chest, and lead to the collection of fluid in the right pleural cavity, or to œdema of the right lung; it may interfere with the action of the heart, and it may press on the inferior vena cava and cause œdema of the feet, enlargement of the superficial abdominal veins, and albuminuria. The urine often contains bile, and an excess of lithates. The spleen is not often enlarged. Thrombosis of the internal saphena vein is not uncommon, and there may be slight pyrexia.

Diagnosis.—Carcinoma of the liver is difficult to diagnose with certainty, if no primary seat of growth can be detected, and if no enlargement of the liver can be made out; but should the primary seat be discovered, carcinoma of the liver may from the jaundice, etc., be diagnosed, even if the organ is not enlarged. But the difficulty usually is to determine whether

a patient with a large liver, but in whom the primary seat of the growth is not obvious, is or is not suffering from carcinoma of the liver. We have first of all to bear in mind the many fallacies connected with an estimation of enlargement of the liver. Having decided that the organ is enlarged, we next have to think of all the causes of enlargement of the liver. These are passive venous congestion, passive portal congestion, the active congestion of hot countries, malaria, yellow fever, leukæmia, Hodgkin's disease, pernicious anæmia, diabetes, fatty liver, hydatid, tropical abscess, the single large abscess met with in those who have never been abroad, suppurating hydatid, actinomycosis, tuberculous abscess, obstruction of the common bile duct, lardaceous disease, hypertrophic cirrhosis, congenital syphilis, and acquired syphilis.

The majority of these diseases never present any difficulty; but it is not uncommon for cirrhosis, with an enlarged liver, or syphilis, to cause hesitation, and in rare cases hydatid and obstruction of the common bile duct give rise to error.

In cirrhosis the nodules are never larger than a small cherry, and therefore the hepatic enlargement is more uniform; they are never umbilicated, neither they nor the whole liver alter in size in a few days, and pain and tenderness are not prominent symptoms. The jaundice is never as deep nor as green as it commonly is in growth, the spleen is commonly enlarged; but the gall bladder is rarely distended, and the stools are not completely clay-coloured. A patient with cirrhosis and an enlarged liver usually dies sooner, after the onset of jaundice and ascites, than does the sufferer from cancer of the liver.

The liver in congenital syphilis may closely resemble growth, but the age of the patient will prevent any mistake. Reference to the effects of acquired syphilis on the liver will show that a mistake might well occur if attention were directed only to the physical condition of the liver; but jaundice, ascites, and clay-coloured stools are almost conclusive evidence of growth. Then, too, rapid enlargement of the organ points to growth; but in syphilis, especially if iodide of potassium be given, it may become smaller. Pain and tenderness usually indicate growth, although the local perihepatitis which is sometimes associated with syphilis may cause pain. Of course attention must be paid to the history and general symptoms.

The main points of distinction between cancer of the liver and chronic blocking of the bile duct by gallstones, or by surrounding inflammation, are that in these conditions the patient does not look as though he were suffering from cancer; the hepatic enlargement is uniform, never so great as it often is in cancer, and the jaundice does not become dark green.

Treatment.—If the diagnosis is correct, the patient must die before many months, and often death takes place sooner. Treatment can only be palliative. Morphine should be used freely, if pain or pruritus are severe. It is possible that in some cases in which the gall bladder is enlarged, the patient may be somewhat relieved by forming a connection between this structure and the intestine; but it is obvious that suitable cases must be very rare. Mayo Robson has successfully excised a nodule of growth from the liver, but this is hardly ever feasible.

PRIMARY CARCINOMA OF THE LIVER.

The proportion of undoubted primary to secondary carcinoma of the liver is about one to twenty-five. Early writers thought primary cancer of

the liver much commoner, out that is because they sometimes overlooked the primary seat, and also because they were unaware that it was often in the gall bladder.

Morbid anatomy.—There are three forms of primary cancer of the liver. In the most common the new growth is deposited in nodules, and the whole liver exactly resembles the organ which is the seat of secondary deposits. In another class of case, the growth consists of one large tumour of the liver. A very good instance of this is recorded by Bright in his monograph on abdominal tumours. In the third variety the cancer cells are uniformly diffused through the liver, and there is a great increase of fibrous tissue in all directions. This often contracts, so that, although at first the liver is increased in size, it gradually becomes smaller.

Symptoms.—Primary carcinoma of the liver is a disease of adult life and generally of old age. Unlike secondary cancer, it is rather commoner in men than women. In no respect does physical examination of the liver reveal any difference from secondary cancer of it. Jaundice may be absent all through the illness; if present, it usually comes on late, and we never meet with the long lasting dark staining which is so common when the organ is affected secondarily; this is probably because the disease is, as a rule, rapidly fatal. In about a third of the cases, ascites may be detected during life, and slight pyrexia is rather more common than in the secondary form. The patients are often wasted, sometimes they vomit, frequently they are constipated, but the stools are never clay-coloured. The urine may contain a trace of bile and even a little albumin.

Diagnosis.—This should be made very cautiously, and is usually incorrect, for the case which is supposed to be one of primary carcinoma of the liver commonly turns out to be one of secondary disease, in which the primary focus has been overlooked. The chief points to which attention should be paid are that, in the primary form the disease is much more rapid, the jaundice is not deep, and the motions are less pale.

Prognosis.—I have analysed a collection of cases of primary carcinoma of the liver, and the remarkable fact comes out that no case lived more than four months after the first symptom appeared, and that the average duration was only twelve weeks.

PRIMARY CARCINOMA OF THE GALL BLADDER.

This is not nearly so rare as was formerly supposed. Most authorities agree that often it owes its origin to gall stones, which are present in 95 per cent. of all the cases, and this explains the fact that it is four times as common in women as in men. Secondary deposits in the liver and the portal glands are very common, and therefore the symptoms are much the same as those of secondary carcinoma of the liver, except that in 68 per cent. of the cases a definite tumour can be felt in the region of the gall bladder, and frequently there is a history of gallstone colic. The growth often spreads directly to the liver, stomach, and colon.

PRIMARY CARCINOMA OF THE BILE DUCTS.

This is a rare form of growth, it is nearly always a cylindrical-celled carcinoma; and when it occurs in the liver, it is, until a histological examination is made, usually confounded with primary carcinoma of the organ. When it takes place in the ducts outside the organ, the ducts be-

hind it and the gall bladder become very distended. It is about equally common in men and women. The chief symptoms are deep jaundice, pain, uniform enlargement of the liver, which usually contains but few secondary nodules. These are just the cases of cancer in which cholecystenterostomy is most likely to relieve the distressing symptoms due to the circulation of bile in the blood, and therefore to make the patient's end less distressing.

SARCOMA OF THE LIVER.

This may be either primary or secondary. The primary form is excessively rare, and cannot be distinguished during life from primary carcinoma, and even after death it may be difficult to decide. Secondary sarcomata reproduce exactly the form of the original growth; they are rarely diagnosed, for the patient usually dies before they give rise to any symptoms.

PIGMENT TUMOURS OF THE LIVER.

These may be carcinomata or sarcomata, either primary or secondary. They only differ from the growths already described in being coloured black, and therefore melanotic growths of the liver can only be diagnosed during life, when the primary growth is known to be melanotic. It is not uncommon in such cases to find only some of the hepatic tumours pigmented.

ANGIOMA.

This occurs with comparative frequency, and forms a small ruddy body, varying in size from that of a filbert to a walnut. It consists of dilated vessels, and is a subject of almost purely pathological interest.

SECONDARY AFFECTIONS OF THE LIVER.

PASSIVE HYPERÆMIA.

When the flow of blood through these organs is impeded, the increased backward venous pressure is often felt very severely in the liver, which becomes uniformly enlarged—it may reach the umbilicus—and tender; if the stretching of it has been rapid, the hepatic pain is very severe. The patient may be slightly jaundiced; he sits upright so as to take the weight of the enlarged liver off the heart and lungs; and in extreme cases of cardiac disease, venous expansile pulsation may be appreciated in the liver, if it is held back and front between the hands, care being taken that the pulsation felt is not that directly transmitted from the aorta or heart. When this backward congestion has lasted some time, the liver is seen after death to be like a nutmeg, because the distended hepatic vein shows up very dark in the centre of the lobule, the liver cells atrophy, those towards the centre of the lobule become dark and bile-stained, while those at the periphery are pale and fatty. The organ is usually hard, and there may be some increase of fibrous tissue, but this is never sufficient for the condition to be mistaken for the disease already described as cirrhosis. If the congestion is long continued, there may be so much atrophy of liver cells and such dilatation of veins that there are shrunken patches containing cavernous tissue; and if these are near the surface, little clumps of dilated venules project from the free surface of the liver, which may weigh less

than normal, and is then said to be in a condition of racemose atrophy. The pain of this form of congestion of the liver is often much relieved by leeches applied over it and a dose of calomel.

FATTY DEGENERATION.

Some amount of fat is found in the livers of persons who have enjoyed perfect health, and a considerable amount is often seen in cirrhosis, but often a great excess of fat is the only abnormal feature of a liver. The organ is then soft and flabby, the edge is rounded, the cut surface is more yellow than normal, the liver substance breaks down easily under the finger, and occasionally it will float on water. Histologically, it can easily be seen that the liver cells are loaded with fat, and in the early stages those at the periphery of the lobule are most affected. During life the uniformly enlarged liver may often be felt to have a smooth rounded edge and a soft feel. It is neither painful nor tender, and we do not know of any symptoms which can be ascribed to fatty degeneration of the liver. The chief causes for a fatty liver are alcoholic excess and phthisis, or indeed any long-standing wasting disease. Very often a general over-indulgence is operative. We often see the liver of confirmed drunkards free from cirrhosis, but very fatty; but we are quite ignorant why alcohol sometimes leads to cirrhosis and sometimes to a fatty liver. Phosphorus causes extreme fatty degeneration of the liver.

WAXY DEGENERATION.

In the liver, as elsewhere, the deposition of lardaceous material takes place first in the walls of the minute arteries, later it spreads to the liver cells; consequently, in the earlier stages of the process, it is seen in the middle of the lobule, but later most of the cells are affected. The weight of the organ is much increased, it may reach 14 lb.; it is smooth, uniformly enlarged, hard, and shows very well the anatomical depressions and surfaces. It cuts like bacon, the surface is dry; a thin section is translucent, and shows the individual lobules very well. During life it is easy to feel, and may reach down well below the umbilicus; there is no pain or tenderness over it, unless there is some coincident perihepatitis; and a lardaceous liver never causes jaundice or ascites, but we can usually find evidence of lardaceous disease of the spleen, kidney, or intestines. Long-standing suppuration, which in the medical wards is usually pulmonary, and due to phthisis, and syphilis are the only known causes of lardaceous disease, but a few cases are occasionally seen in which no cause can be discovered. Once I have seen it due to congenital syphilis, but this is very rare. The diagnosis may be very difficult when lardaceous disease accompanies cirrhosis or hepatic syphilis, for the liver is then no longer smooth.

SYPHILIS.

If acquired syphilis affects the liver, it produces such characteristic appearances, that, if they are seen in the post-mortem room, they render it absolutely certain that the patient has had syphilis. The changes are of two kinds, gummatous and fibrous. Many gummata, even fifty, may be deposited throughout the liver, and they often project on its surface, and are always sharply localised. The early stages are

rarely seen; usually we meet with a yellowish gummatous mass. In quite exceptional cases this liquefies, and it may then burst, still more rarely it calcifies. Each gumma is surrounded by a zone of new-formed fibrous tissue, which sends wide fibrous branching bands radiating in different directions through the liver; but the hepatic substance between the bands is healthy and possibly hypertrophied, to compensate for the destruction of liver tissue. If the gumma was originally very small, or has become so from absorption, we see several branching bands radiating from a centre, the gummatous origin of which is not obvious, and indeed it is said that these fibrous radii may form apart from gummata. In time the fibrous tissue contracts, and a depressed fibrous patch on the surface of the liver, and from which bands radiate into the organ, is very typical of syphilis. These depressions, those caused by the absorption of gummata and the projecting gummatous nodules, make the surface very knotty and irregular. The microscope often shows some diffuse fibrous change, but usually it cannot be seen by the naked eye, and the principal bands are so wide and characteristic that it is easy to tell a syphilitic liver from one affected with cirrhosis. There may be some lardaceous change.

During life the liver may be felt to be enlarged, hard, and irregular; the size of some of the gummatous nodules may be observed to diminish under treatment; and the patient may complain of pain and tenderness in the hepatic region, due to some patchy perihepatitis. Jaundice is excessively rare; it may be caused by coincident catarrh of the ducts, to the pressure of a gummatous gland, or to pressure from cicatricial contraction. Ascites, too, is hardly ever seen. Carcinoma, cirrhosis, and cirrhosis combined with syphilitic deposits in the liver, may all of them be exceedingly difficult to diagnose from syphilis of the liver, especially if it is lardaceous, for then it is much enlarged.

Congenital syphilis, as far as I know, never produces effects on the liver which are seen in adult life. It may cause exactly the same results as acquired syphilis, and I have seen them well marked in a child 8 years old; but it most often produces another effect, which is usually seen in children who are still-born or die shortly after birth. The organ is then enlarged, stony hard, inelastic, flint grey, and anæmic. A section is smooth and homogeneous, and the outline of the individual lobules cannot be seen, but they are represented by whitish spots. The alteration consists in a great hyperplasia of the young connective tissue, and is most marked in the neighbourhood of the portal vein, the walls of which may become so thick that a bristle cannot pass down it; these changes vary much in intensity in different cases and in different parts of the liver in the same case.

ACTINOMYCOSIS.

The ray fungus may grow in the liver, and sometimes this may be the only organ affected. The effects produced are in all their stages very like those caused by slow tuberculous lesions. First, there is a small granulation tumour; this grows till it may be as big as a fist; the connective tissue around it proliferates, while the growth degenerates in the centre, where it finally breaks down and discharges pus. When these growths occurred in the liver, they were always described by the older writers as tuberculous, and indeed they can often only be distinguished either by noticing the very bright yellow, glistening, little masses of ray fungus, each smaller than a pinhead, which may be observed in the pus or

by searching with the microscope for the fungus; but the fact that the abscess cavity is much trabeculated, and there is but little caseation, may at the first glance suggest actinomycosis rather than tubercle. During life the patient would complain of hepatic pain and tenderness, and we should observe symptoms of chronic suppuration, with perhaps evidence of local swelling in the liver, and if the pus were discharged we should find the ray fungus in it.

TUBERCULOSIS.

It is common at a post-mortem examination to see small grey miliary tubercles scattered on the surface and substance of the liver, and one or two cases are on record in which jaundice has been associated with acute miliary tuberculosis of the liver. Many French authors have given an account of cirrhosis following these depositions, and have also described a tuberculous cirrhosis occurring without the deposition of tubercle in the liver, but I cannot help thinking that the French school have much exaggerated the importance of tuberculous cirrhosis. Very rarely the liver may contain several small caseous tuberculous abscesses, and in still more exceptional cases large tuberculous caseous abscesses occur in it. I have seen one such case, and one has been successfully operated on by Mayo Robson. It is only when these large abscesses form that tubercle of the liver becomes of clinical interest; and an abscess should never be stated to be tuberculous till the bacillus has been found, for abscesses due to actinomycosis are much like those due to tubercle. In advanced cases of phthisis the liver is often lardaceous or fatty, and it may be swollen from obstructed pulmonary circulation.

HYDATID OF THE LIVER.

Etiology and pathology.—This disease of the liver is due to the swallowing the ova of the *T. echinococcus.* This tape-worm is rather less than a quarter of an inch long, and when fully developed consists of four segments; the most anterior (the head) is small, and has four sucking discs and a rostellum of from thirty to forty hooklets; the last three segments are called proglottides; the second and third are quite small, but the posterior is larger than the other three together, and alone contains sexual organs. This tape-worm inhabits the alimentary canal of the dog, and its ova are discharged in the fæces; hence hydatid of the liver is commonest in Iceland, where dogs live in the same huts as the inhabitants. It is often seen in Australia, where dogs are used for herding sheep, and it is by no means rare in England. In Iceland it is more common in women, as they clean the dogs; in Australia it is met with chiefly in men, as there they are brought most into contact with dogs. In the last seven years, there have been sixteen cases in Guy's Hospital. No age is exempt. When the ova have been swallowed by man, their shell is dissolved; the contained embryo or scolex, which has six little hooks arranged in two rows, bores its way into the wall of the stomach or intestines, and from there may be carried to any part of the body, but most frequently it is taken by the portal vein to the liver. Of 1862 cases quoted by Osler, the parasites existed in the liver in 953, in the intestinal canal in 163, in the lungs or pleura in 153, in the kidneys, bladder, or genitals in 186, in the brain and spinal cord in 127, in the

bones in 61, in the heart and blood vessels in 61, in other organs in 158. It becomes stationary in some part of this organ, loses its hooks, and gradually becomes a cyst containing clear fluid. The wall of this cyst thickens, and consists of pearly white translucent layers. The outer, the thicker, is laminated, and, when torn, curls back in the reverse way to its natural curve; the inner layer is granular, and is said to contain muscular fibres. The hepatic tissue around a cyst is compressed and becomes converted into a thin layer of fibrous tissue, but the hydatid cyst is not in continuity with this, and can always be shelled out from it. On the inner surface of the cyst a number of minute projections form; these, under the microscope, are found to be scolices or heads, exactly like the first joint of the *T. echinococcus*, and they usually undergo cystic degeneration, and form cysts exactly like the original cyst, which has therefore a number of daughter cysts in its interior; these become detached from the parent wall and lie free in the parent cyst. The process may be repeated, and grand-daughter cysts form in the daughter cysts, and again repeated, till there is a number of cysts one within the other. But there comes a stage when the cysts remain attached to the wall of the parent cyst by a pedicle; they are then called brood capsules, because a number of fully-developed heads or scolices, each complete with suckers and hooklets, grow from the interior surface of the cyst and project into its interior. These are usually arranged so that the suckers and hooks are turned inwards. The fluid of these cysts is clear, limpid, of a low specific gravity—under 1010; it contains chloride of sodium and occasionally a trace of sugar, and of succinate of ammonium but no albumin, a fact by which it is easily known from pleural and peritoneal effusion. A few scolices, several hooklets, and even fragments of laminated membrane, may often be seen in it on microscopical examination. A hydatid of the liver may become very large; it may be almost as large as the liver itself; the hepatic tissue being reduced to a thin layer all over it; or it may form a tumour as large as a man's head, projecting from the liver. It may contain several pints of fluid and hundreds of daughter and grand-daughter cysts, but it is rare in man for a liver to contain more than one hydatid tumour. Not infrequently hydatids die, the fluid is then absorbed, the parent cyst contracts, and is ultimately filled with much bile stained putty-like matter, mixed with calcareous salts and glistening cholesterin crystals, a number of empty cysts compressed together, and many hooklets, which, being calcareous, have escaped disintegration. Death of the cyst usually takes place while it is still rather small, and so dead hydatids are often found in the post-mortem room, when there was nothing during life to indicate their presence. The fibrous surrounding of dead hydatids becomes very dense and often calcareous. Sometimes the original cyst produces no daughter cysts; it is then called an acephalocyst hydatid.

Very rarely the daughter cysts bud off externally instead of internally, and as this process goes on indefinitely the liver may become riddled with hydatid cysts, and they may even extend to neighbouring organs. I have known a hydatid originating in the liver to grow in this way into the pleura, which became full, and was found to contain many hundreds of these cysts. In this case, failure to boil the fluid extracted with an exploring needle, led to an erroneous diagnosis of simple pleuritic effusion.

Multilocular hydatid, which is excessively rare, was always regarded as a cystic form of malignant disease, till Virchow in 1855 first showed

its true nature. It forms a solid globular mass in the liver; it may be 6 in. in diameter. It can be shelled out of the organ. On section, it contains numerous smooth-walled cavities, about the size of small peas or smaller, having in them gelatinous fluid, which has in it many hydatid membranes compressed together; and usually some scolices can be found, if looked for carefully. A series of sections show that these cavities communicate with each other. Multilobular hydatids are always found to be softening in their centre. Their mode of development is not thoroughly understood. It has been suggested that in this form of hydatid the parasite occupies the interior of the lymphatics.

Symptoms.—These may almost be inferred from the above description of the cause of the disease. A hydatid of the liver, if it does not suppurate or rupture, can hardly be diagnosed unless it produces an enlargement of the organ. This may be detected either by palpation or percussion; it is confined to one part of the liver, most often the right lobe, and is rounded and smooth, but neither painful nor tender. If it begins near the edge of the liver, and grows very large, it may require considerable care to demonstrate that it is connected with the liver at all; on the other hand, if it starts in the interior, a large hydatid may produce little alteration in the shape of the liver. Even if the tumour is accessible, the feel of it may vary much, sometimes distinct fluctuation may be obtained, at others the cyst is so tense that it feels quite hard. Much attention has been directed to the "hydatid thrill," but it is often absent, and may be occasionally felt in any tense cyst whatever its origin. To obtain it, a finger of the left hand is placed on the cyst and struck with one of the fingers of the right hand, the left finger may then feel a distinct thrill under it. Ascites, enlargement of the spleen, œdema of the lower extremities, albuminuria and jaundice, are all accidental and very rare symptoms; they form no part of the clinical picture of hydatid of the liver, and they indicate that the cyst presses on the portal vein, the inferior cava, or the bile duct, as the case may be. A hydatid cyst has been known to rupture into the bile ducts and cause jaundice, into the gall bladder and produce biliary colic, or into the portal vein or the inferior cava. The latter accident causes instant death. If an exploring needle which has been thrust into the hepatic tumour draws fluid which has the characters of hydatid fluid, the diagnosis is certain. As already mentioned, a hydatid may die, but if left alone it is always liable to rupture, either spontaneously or subsequent to a blow. This rupture may take place, not only in the direction just mentioned, but also into the pleura or lung, into the peritoneal cavity, into the stomach, into the intestine, into the urinary passages, into the pericardium, or externally. Rupture into the pleural cavity or lung is the commonest, and rupture in any direction is usually either fatal immediately or later on, as a result of the suppuration induced. Hydatid cysts may also, if left alone, kill by pressure upon important organs, or by exhaustion; not infrequently they suppurate (see "Abscess of the Liver"); and lastly, death may be due to implication of other organs by the rare form of hydatid which buds externally. It must not be forgotten that sometimes several organs may be simultaneously affected with the common forms.

Diagnosis.—A hydatid at the upper part of the right lobe of the liver may, if it suppurate, easily be confounded with an abscess between the liver and diaphragm. A non-suppurating hydatid in this position has often been mistaken for pleuritic effusion, but the upper limits of the

fluid in pleuritic effusion is horizontal, while that of the hydatid is dome-shaped. The diagnosis from encysted pleuritic effusion may be very difficult, but nearly always a supposed right-sided encysted basal pleurisy turns out to be a hydatid cyst growing from the liver. A distended gall bladder is distinguished from a hydatid cyst by its position, its shape, the history of colic, and by the fact that jaundice is usually present. But the distinction is often far from easy, and I have seen the mistake made when every care was taken to prevent it. It should not be forgotten that a hydatid cyst may, by rupturing into the gall bladder, cause symptoms very like those of gallstones. A deep-seated hydatid may be difficult to distinguish from a lardaceous liver, especially if this has in it syphilitic fibrous tissue and gummata. Fagge points out that such livers do not move freely on respiration, owing to adhesions, and there is often some pain and tenderness, but the liver with a hydatid in it moves freely, and is neither painful nor tender. The diagnosis of hydatid from cancer may generally be made from a consideration of the whole of the symptoms of the case. A renal cyst may easily simulate a hydatid tumour of the liver, but to avoid a mistake attention must be paid to the origin of the cyst and the direction of its growth, to its movement with respiration, and to the presence of the colon in front of it. Unfortunately, it may be so large that its origin cannot be determined; a renal cyst may, owing to the attachment of the kidney to the liver, move on respiration, and the colon may be empty. I have seen a phantom tumour of the rectus so closely resemble a hydatid of the liver that the diagnosis could not be made until chloroform had been administered. In all these cases of difficulty the examination of the fluid withdrawn by an exploring needle will settle the diagnosis.

Prognosis.—As old dead hydatid cysts are found post-mortem, it is clear that sometimes the disease undergoes a spontaneous cure. We have no knowledge of the cause of this, nor do we know how long a hydatid can live, although we do know that their growth is very slow. Considering the risks from rupture and suppuration, it is generally allowed that if a hydatid of the liver has been diagnosed, surgical interference is necessary.

Treatment.—Simple aspiration which does not require an anæsthetic may certainly sometimes kill the parasite, and lead to a complete cure without any re-collection of the fluid, but often it does re-collect, sometimes the dead hydatids induce suppuration, and it is usually very difficult to say whether or not the case is cured. The technique of free incision into the cyst has been improved so much of late years, that most surgeons prefer to expose the liver over the cyst, stitch it to the abdominal wall, pack carefully around it, then evacuate the cyst, and leave in a wide drainage tube. As the escape of a little hydatid fluid into the peritoneum does no harm, it is usual to do all the operation at one sitting; but if there is no urgency, the opening may be deferred after the stitching of the cyst to the abdominal wall, until adhesions have formed. As far as possible, all the cysts and membrane should be removed at the time of operation; if, however, all cannot be taken away, those that are left will usually be discharged in a few days. The seat of operation will be determined by the position of the hydatid. Those at the back of the liver, which cannot be reached except through the pleura, may be evacuated through the pleura, but they require considerable skill and judgment in their surgical treatment.

In very rare cases, erythema or urticaria, either of which may be very extensive, has appeared on the body after tapping a hydatid cyst, and generally the rash is accompanied by a high temperature and abdominal pain. Sometimes, too, the patient may, after the tapping, be seized with faintness, dyspnœa, and vomiting; he becomes cold, the pulse becomes very weak, and he may die. Both these effects are extremely uncommon. No explanation of them is forthcoming. Some experiments of Roy's appeared to show that hydatid fluid is a respiratory and cardiac depressant; but Graham has failed to confirm this.

OTHER CYSTS.

A hydatid cyst is the only cyst of the liver of any great clinical importance; but there are on record several interesting cases in which cysts, which are certainly not hydatid, have been found in the liver and in other organs in the same patient. Pye-Smith has recorded an example, and I have described cases and given references to the subject. These cysts must never be confounded with the holes in the liver which are the result of decomposition, which may make it look like a sponge.

Several species of flukes have been found in the human liver. A serious endemic disease, due to a fluke, exists in Japan; but in England flukes are only of post-mortem interest. They may be found dead and calcified.

PERIHEPATITIS.

By this term we understand an inflammation of the peritoneal capsule of the liver; it is either acute or chronic. The acute is merely a part of some acute process, such as a hepatic abscess or acute peritonitis.

Chronic perihepatitis is either partial or universal. Instances of partial perihepatitis are the local peritonitis, which occurs round a thickened gall bladder, and that seen over a gumma. Partial perihepatitis is also often present on livers enlarged as a result of disease of the heart or lungs. This variety of perihepatitis is of little clinical interest. Universal perihepatitis is a condition in which the whole capsule of the liver is thick, opaque, and white.

Etiology. — The condition is almost always associated with and a part of general simple chronic peritonitis. I took from the post-mortem records at Guy's Hospital, quite at random, forty cases of perihepatitis. Eighteen were examples of partial, twenty-two of complete perihepatitis. Of these twenty-two, in two it was stated that there was no peritonitis, in seventeen there was peritonitis, and in the remaining three there is no mention of the peritoneum. In none of the seventeen was the peritonitis due to tubercle or growth; but it was always that chronic form in which the peritoneum becomes thick and opaque, the omentum puckers up and forms a thick, hard mass, and the mesentery shrinks and drags the intestines back to the spine. The intestines may be so matted together that they can be removed *en masse.* These facts prove the statement just made, that universal perihepatitis is nearly always part of a general simple chronic peritonitis. As in nineteen out of the twenty-two cases the kidneys were granular, we

must regard Bright's disease as being perhaps the most important cause of perihepatitis; perhaps, also, syphilis is a cause, for two of the remaining three cases had suffered from syphilitic symptoms.

The liver is rarely enlarged; but if the lower edge of it can be felt, it is thick, rounded, and uniform. The other signs of chronic peritonitis and of chronic interstitial nephritis are usually present. The most important sign of chronic peritonitis is ascites, which requires frequent tapping, because the fluid re-collects after it has been withdrawn. Thus I have known a case tapped thirty times; indeed, chronic peritonitis is by far the most common cause of ascites that needs frequent tapping. The puckered thickened omentum may be felt as a hard mass lying across the abdomen, just above the umbilicus, and as the ascitic fluid collects, the abdomen quickly becomes dull all over, because the intestines are drawn back by the puckering of the mesentery. If the fluid becomes loculated in and among the coils of intestine, where it may be shut off by peritoneal adhesions, the case may be very difficult to diagnose. The average age at death among my cases was 47½ years. The youngest was 29, the eldest 68. The proportion of males to females was as thirteen to eight.

Morbid anatomy.—The white jacket of the liver, which often has little pits on it, may be a quarter of an inch thick; it easily peels off the surface of the liver, which is quite smooth, and the inferior edge of it may be folded up on to the anterior surface of the organ and fixed in this position by the jacket. The hepatic tissue is, according to Fagge, commonly soft, and is very often loaded with fat. It is seldom cirrhotic, but there is sometimes an excess of fibrous tissue in the course of the large portal vessels. The liver with its thickened capsule usually weighs between 50 and 60 oz., from which we may conclude that the organ itself is somewhat atrophied. The thickened capsule does not exert enough pressure to cause jaundice, and the ascites is to be ascribed to the peritonitis and not to pressure on the portal vein, for I have by dissection proved that this is not compressed by the thickened hepatic capsule.

Diagnosis.—These cases are usually confounded with cirrhosis; but in perihepatitis jaundice is absent, the signs of chronic peritonitis are present, and the patient usually survives several tappings. Reference to the description of cirrhosis will show that this last fact is very strong evidence of chronic peritonitis rather than ascites.

Treatment.—The abdomen must be tapped as may be necessary. No drug is known to be beneficial, but iodide of potassium may be tried.

W. HALE WHITE.

DISEASES OF THE PANCREAS.

IN order to obtain some information as to the relative frequency of disease of the pancreas, I searched the records of the post-mortem examinations made at Guy's Hospital for the twelve years 1883–1894 both inclusive, during which period almost 6000 post-mortem examinations were made. Once an accessory pancreas was found, and on ninety-nine occasions (or in 1·6 per cent.) the organ appeared to the morbid anatomist to be diseased. The following table gives a summary of the ninety-nine cases :—

Cirrhotic, congested, or hard pancreas	20
Primary malignant disease of pancreas	19
Small pancreas	16
Secondary deposits of growth in pancreas	11
Fatty pancreas	8
Malignant growths of other organs adherent to pancreas . .	7
Pancreatic cysts (including one case of hydatid)	4
Pancreatic calculi	3
Floor of ulcer of stomach formed by pancreas	3
Tubercle of pancreas	2
Dilatation of pancreatic ducts not due to growths	2
Floor of ulcer of duodenum formed by pancreas	1
Ruptured pancreas from cart wheel	1
Abscess in pancreas	1
Œdema of pancreas from heart disease	1
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	99

CIRRHOSIS.

When the pancreas is congested and hard, the condition is nearly always the result of long-standing venous pressure. In eleven, or rather over half the cases, this was due to disease of the heart, and then the liver was usually nutmegged; in a much smaller number it appeared to be caused by disease of the lung. In two at least it was associated with cirrhosis of the liver, in one there was an enormous ovarian cyst, which might well have exercised pressure on the portal vein, in another a large mass of portal glands infiltrated with growth pressed upon the portal vein. It is impossible to classify the causes more exactly, for sometimes, as in cases with advanced phthisis and cirrhosis of the liver, it is difficult to assign the share in the causation of the hardness of the pancreas correctly among those organs, disease of any one of which might have been the cause. The important fact is that in one out of every three hundred post-mortem examinations, the pancreas is congested and hard from backward venous pressure. Microscopically, there is a great increase in the amount of fibrous tissue, usually it lies between the lobules, but it may extend into them ; there is also considerable small-celled infiltration. I have once known the pancreas to be so hard, and so easily felt after the abdomen had been tapped, that it was mistaken for a mass of malignant disease. In three cases of diabetes the pancreas was especially hard. Riedel has in very rare cases noticed a chronic inflammatory enlargement of the head of the pancreas in association with gallstones, and no doubt due to the irritation of their passage.

ATROPHY.

In thirteen out of sixteen cases the patient suffered from diabetes, and this is the commonest pancreatic condition found associated with diabetes. Sometimes the organ only weighed an ounce. Usually it was described as soft and flabby, but in a few instances it was hard. In two of the remaining three cases there was much abdominal malignant disease, so that there may have been much interference with the blood supply of the pancreas, and the third patient was an old woman, who died, shortly after admission, from the effects of a severe burn.

FATTY CHANGES.

In all these eight cases the infiltration of the pancreas with fat was evident to the naked eye. Two of the patients were young (7 and 16 years old), and both had mitral disease with backward pressure. Six were elderly, their average age being 66. Five of these were surgical cases. A study of all eight cases appears to show that there are two groups—one in which a fatty pancreas is associated with backward pressure, and another, comprising elderly persons, who are bad surgical subjects, and who usually have evidence of degeneration of other viscera.

CALCULI.

As these were only found three times in 6000 post-mortem examinations, they are clearly very rare.

From a study of these cases, and others scattered through literature, it appears that pancreatic calculi are usually composed largely of carbonate of lime—although the pancreatic secretion contains none; they are white in colour; sometimes rounded, but often branching coral-like masses; the ducts in the organ are nearly always dilated, for the most part uniformly, but sometimes they form small cysts containing a white mucoid fluid. Very often the pancreas is hard and indurated, containing an excess of fibrous tissue, apparently as a result of the obstruction of the duct by the calculus. Large cysts and abscesses are very rare. By far the greater number of the patients are males over 40 (the three Guy's cases were all males, and their ages were 70, 58, and 55). Pancreatic calculi have been found in the fæces, but apart from this it is hardly possible to diagnose their presence during life. There is very little evidence that they cause colic; some of the persons in whom they have been found have had glycosuria. Vomiting has been present in some cases, and it is stated that the fæces may contain much fat, and that there may be diarrhœa with fatty stools. They have been known to produce jaundice from impaction in the duodenal orifice.

It will be noticed that in the list of ninety-nine cases, two are given of dilated pancreatic duct; one, in which jaundice was present, was fatal, owing to an unsuccessful cholecystenterostomy; the duodenal orifice was found closed by an old cicatrix; in the other, the pancreatic ducts were dilated without obvious cause. In one of the cases of pancreatic cyst there was a small cavity in the head which opened into the duodenum; the view

taken at the autopsy was that a small abscess in the pancreas had ruptured into the duodenum, and as the patient died of hæmatemesis and melæna, most likely in so doing it opened a vessel. All these cases probably represent the after effects of calculi.

MALIGNANT DISEASE.

Primary.

This is rare, occurring once in about every three hundred autopsies.[1] The proportion of males to females is two to one. As pancreatic calculi are commoner in men, it may be that they by their irritation can induce malignant disease of the pancreas; but as they are so exceptional, this cannot be common. Sarcoma is very rare; it occurred once in the nineteen cases from Guy's; this patient was æt. 28. The patients afflicted with carcinoma were usually between 40 and 60. The youngest was 33, and the oldest 73. The growth is nearly always limited to the head of the gland, it may be quite large; one tumour measured 9 in. across, but this was of exceptional size. Scirrhus is much more common than medullary carcinoma. It is probable that as in the liver so in the pancreas, the primary seat of the growth may occasionally be in the ducts. Cancerous growths of the pancreas have been known to undergo colloid degeneration. Bright records cases in which they ulcerated into the duodenum; and a patient of mine died from hæmatemesis, due to an ulceration of a cancer of the pancreas into the stomach. Secondary deposits may occur almost anywhere, but by far the most common seats are in the portal glands and the liver. One of the nineteen cases I have collected showed considerable fat necrosis of the omentum. It is very important to remember that either by pressure of the enlarged portal glands, or by the direct pressure of the original tumour in the head of the pancreas, the patient may be jaundiced and the bile ducts dilated; and in at least a third of the cases the gall bladder is considerably distended, and the liver itself may be enlarged. The pancreatic ducts, too, are often dilated. The most frequent symptom is constant severe abdominal pain; usually the patient says it is deep down above the umbilicus, but in one case it was referred to the back. Vomiting, which in most cases is very difficult to treat successfully, and which bears no relation to food, is common. In about half the cases there is obvious wasting, and this may be very marked. The bowels are constipated, and if the patient is jaundiced the stools may be clay-coloured; and, as Bright pointed out many years ago, the motions may contain large quantities of fat—it may be so abundant, that it forms a thick scum, particularly about the edges of the vessel containing the fæces. As an obstruction of the common bile duct is so frequent, and this kind of motion is so rare, it is likely, as taught by Gairdner, that it is due to blocking of the pancreatic duct. This probably bears on the statement, which I can confirm from personal observation, that the subjects of pancreatic cancer die sooner and waste more rapidly than most sufferers from carcinoma. These patients are usually markedly anæmic, and if there is œdema of the ankles it may be due to this, or to pressure on the inferior vena cava.

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[1] Mayo Robson has recently suggested that some cases of supposed malignant disease of the liver are examples of chronic pancreatitis, and he has enlarged our knowledge of this condition.

The tumour may be so large that it can be seen; thus the report of a case under Pye-Smith says, there was a large globular swelling in the right epigastric region bulging the ribs. This turned out to be a malignant growth at the head of the pancreas as large as a fœtal head. If it cannot be seen, the tumour may in many cases be felt as a hard immobile mass, usually tender, and having transmitted pulsation from the aorta, and resonant if the stomach or colon in front of it contains gas. The abdominal muscles on the right side are often rigid. The enlarged liver and gall bladder may be easy to feel. But still it must be remembered that often malignant disease of the pancreas is suspected because the patient has abdominal pain, vomiting and wasting, for which no other cause can be suggested. Recently, from these symptoms in one of my patients this diagnosis was made, although no growth could be felt even under chloroform. The gall bladder was not dilated, and there was no jaundice. The diagnosis turned out to be quite correct, the pancreatic growth being confined to the tail of the gland.

The symptoms due to the spread of the growth are not numerous. In a case of my own, it grew so much to the right that the calibre of the duodenum was very much diminished, and no doubt the patient's constipation and vomiting were partly referable to this. Not long ago, a patient was admitted into the hospital for intestinal obstruction, caused by a growth of the colon. It was found that the primary disease was in the head of the pancreas, and the growth in the colon was only due to direct spreading of the growth from the pancreas. In another instance besides that previously mentioned, the stomach was affected in a similar way. I have seen the semilunar ganglia extensively infiltrated in a case of scirrhus of the pancreas.

Little good is gained by a long account of the differential diagnosis. Mistakes are most often avoided by those who are most thorough and careful in their examination. I have known a patient in whom a malignant growth in the pancreas, which did not spread to the bowel, produced such extreme constipation that he was operated on for intestinal obstruction; and in another patient with the same disease, the constancy of the pain, the jaundice, the distended gall bladder, and the vomiting, led to an operation because he was thought to be suffering from an impacted gallstone. It may be very difficult to decide whether the case is one of carcinoma of the pylorus or of the head of the pancreas; malignant disease of the colon or gall bladder may give rise to error, and primary malignant disease of the pancreas may be overlooked as a cause for secondary deposits in the liver.

All that can be done is to treat the symptoms. Morphine is very valuable.

SECONDARY GROWTHS.

Six of these eleven cases were carcinomata. The primary growth was in the stomach, sigmoid flexure, rectum, ovary, peritoneum, or breast. In two instances the secondary deposit was in the head of the pancreas, twice the organ was generally infiltrated, once the tail only was affected, and once the tail and head, the intervening portion being free. Four cases were sarcomata, the primary growth being in bone twice and in the mediastinum twice. In one instance the nature of the primary growth is not stated. It is clear that the pancreas is not a frequent seat of secondary deposits.

MALIGNANT ADHESIONS.

In four cases the primary growth was in the pylorus, once in the lesser curvature of the stomach, once in the colon, and once it was sarcomatous in the abdominal glands. Thus we see that almost the only growth likely to be adherent to the pancreas is one in the pylorus.

PANCREATIC CYSTS.

These are very rare. Only three were found in 6000 autopsies at Guy's. One was an example of that curious condition in which cysts are found in many organs in the same patient. In this case they were in the cerebellum, kidney, and pancreas. The duct of Wrisberg was neither obstructed nor dilated. The case is recorded by Pye-Smith, and references are given to the whole subject by Savage and myself. Another was an instance of hydatid of the pancreas; this is excessively rare, and I know of no means by which to diagnose it from the cysts about to be described, unless some of the fluid were examined.

The pancreas is liable to the formation of large cysts, of which our third case was an instance, the causation of which is very obscure. They are not due to blocking of the duct, for no obstruction can be found; the duct is not dilated; when it is compressed by a growth, cysts do not form in the pancreas; and, lastly, when the bile duct is compressed, cysts do not form in the liver. It has been suggested that these cysts are due to injury, but there is no proof of this. They are almost equally common in the two sexes, and may occur at any age, but they are most often met with between 20 and 40. The cyst is very tense, and of large size; it may fill the abdomen, and hold many pints of fluid; one contained 15 litres. It has a specific gravity of between 1010 and 1020, is alkaline, contains between 1 and 3 per cent. albumin, and is generally turbid. The colour has varied much in different cases, in most it has been either green or brown; but white, opalescent, and yellowish red fluids have been described, and it has even been stated to be clear. Usually there is mucin and a sugar-forming ferment in it; leucin, tyrosin, blood pigment, and urea, have all been found in some cases. It may emulsify fats.

A pancreatic cyst could hardly be diagnosed until it is felt; indeed, the patient often does not consult a doctor until he himself notices a tumour, which, if produced by a pancreatic cyst, is smooth, rounded, and tense. It is situated above the umbilicus, and more to the left than to the right of the middle line; the recti are rigid; it cannot be moved about by the hand; it moves but little on respiration, and the edge of the liver is unconnected with it. The great and essential point to determine is its relation to the stomach. This should be distended with gas by giving separately the two portions of a seidlitz powder; and then by percussion, succussion, and palpation, it will be easy to make out that the stomach is in front of the tumour. The colon, too, may be shown to be in front by distending it with water. This is easy, if the buttocks are raised on two or three pillows, and a quantity of water is run into the rectum by means of a long indiarubber tube with a funnel raised considerably above the patient. There is no reason for supposing that when it is small a pancreatic cyst gives rise to any symptoms, but as it grows the patient may complain of pain because the cyst presses or drags upon surrounding structures. Pressure on

the stomach may cause vomiting, with much dyspepsia, and then the patient loses flesh. The bowels may be constipated. In several cases pressure on the bile duct has led to jaundice, varying much in intensity in different cases, because the precise position and degree of distension of the cyst vary. There may be a little albuminuria, and if the destruction of pancreatic tissue is very great, the urine may contain sugar. A distinct increase in the size of a cyst can often be noticed in a fortnight, and if it is tapped the fluid soon collects again. Severe hæmorrhage may take place into a pancreatic cyst, and then the patient may become suddenly collapsed.

It is possible that a peritoneal blood cyst may be in such a position as to closely resemble a pancreatic cyst, and it might be that a diagnosis could only be made by examining the fluid removed by an exploratory puncture. Pancreatic cysts have been mistaken for ovarian cysts, but proper care should prevent this.

When we remember that the stomach and colon are in front of these cysts, it is clear that exploratory puncture from the front is attended by danger. Usually exploration is not necessary, but if it is, the cyst can often be reached by a fine needle, thrust in below and a little behind the tip of the twelfth rib, and as it is retroperitoneal, the peritoneum will probably not be wounded. Unless the patient has diabetes, in which case it would probably be best to aspirate from time to time, these cysts should be laid open and drained by an incision below the outer part of the left twelfth rib. If the patient has not diabetes he generally recovers.

TUBERCLE.

In the two cases mentioned there were caseous nodules in the gland, and both had peritoneal tuberculosis. Tubercle of the pancreas is excessively rare. Gumma of the pancreas is known.

ACUTE PANCREATITIS.

By far the best account of this rare disease is that given by Fitz. He suggests that it is usually due to the extension of a gastro-intestinal inflammation along the pancreatic duct, and he describes three varieties differing in their morbid anatomy and symptoms. A few cases have been recorded in England. I myself have seen one.

HÆMORRHAGIC PANCREATITIS.

This occurs between the ages of 25 and 60, and is commoner in men than in women. About half the patients have been liable to colicky attacks and indigestion. The immediate attack begins suddenly with pain, generally very severe, and most intense in the upper part of the abdomen. Shortly after, the patient begins to vomit, and in most cases he is constipated. Soon (usually in the course of a day or two) he is extremely collapsed, and in most instances he is dead by the third day; life, nevertheless, may be continued to the sixth day, but the patient rarely survives the onset of the collapse more than a few hours. The abdomen may be somewhat

distended and resonant. After death it is seen that much blood is extravasated into the pancreas, and it may also be seen around the organ. There is histological evidence of acute inflammation of it, fat necrosis is seen in its lobule, and often too in the mesentery and omentum, and the pancreatic vessels may contain ante-mortem clot. This disease is liable to be confounded with acute intestinal obstruction, but in pancreatitis the abdominal distension is not great, definite intestinal coils are not seen, the onset of the collapse does not coincide with the onset of the illness, and an enema may bring away fæces. Local tenderness is a point in favour of pancreatitis, very severe vomiting and a dry tongue point rather to obstruction. If, when a laparotomy has been performed, under the impression that the case is one of intestinal obstruction, no distended coils with collapsed coils beyond can be seen, the pancreas should, if possible, be inspected, and if it is diseased the wound should be sewn up, and the patient treated with general stimulants. Osler records such a case, in which the patient made a good recovery, and was well five years later. This disease has been confounded with perforative peritonitis. The previous history (gall-stones, gastric ulcer, appendicitis, etc.), the abdominal distension, the immobility of the abdomen, thoracic breathing, early collapse, and subsequent reaction, and other signs of peritonitis, will help us. Poisoning should always be borne in mind. Every possible means should be adopted to maintain the patient's strength.

SUPPURATIVE PANCREATITIS.

Fitz has collected twenty-one cases. Their ages vary between 20 and 74. Seventeen were males, four were females. Most were chronic. In the acute cases the onset is marked by the sudden supervention of intense abdominal pain and incessant vomiting. At first the bowels are constipated, later there is diarrhœa. Slight fever is noticed about the third day ; the abdomen is then distended and tender, and hiccough is frequent. The patient dies in the course of about a week, and the pancreas is found studded with minute abscesses, many of which have burst into the peritoneum, setting up acute peritonitis. The chronic cases, which often drag on for months, may in their onset exactly resemble these acute cases, or they may throughout behave like a chronic pyæmia ; in the course of a few weeks the upper part of the abdomen becomes tender and rigid, but a distinct tumour is very rare. A circumscribed single abscess of considerable size is usually found. This may open into the stomach, duodenum, or cavity of the great omentum. Pylephlebitis and abscesses of the liver may result, jaundice is occasionally present. Fat necrosis is rare. The abscess in the one case of pancreatic abscess which occurred in the ninety-nine cases of pancreatic disease I collected, was in the head and quite small, and as the duct was dilated it may have been due to a calculus. The patient died of carcinoma of the colon. Pancreatic abscess may be due to septic thrombosis.

GANGRENOUS PANCREATITIS.

This may be secondary to perforative inflammation of the gastro-intestinal or biliary tract, but it usually results from hæmorrhagic pancreatitis, and is fatal in a few weeks. The gangrenous process extends

to the tissues around the pancreas, produces more or less complete sequestration of it, and the sequestrated gland may lie in the omental cavity soaked in pus. Both pus and pancreas may be discharged into the intestine, and at least two cases are on record of recovery after this event. Phlebitis of the splenic vein is common, and the patient may have diabetes. The symptoms are at first those of acute hæmorrhagic peritonitis; later, weakness, slight pyrexia, vomiting, diarrhœa, abdominal distension, and fatal symptoms of collapse are frequent. There may be obvious local tenderness, or even a tangible tumour. If the disease could be diagnosed, the right treatment would be to open the abscess in the way recommended for a pancreatic cyst.

HÆMORRHAGE.

It has already been mentioned that bleeding may take place into pancreatic cysts, but apart from that an apparently healthy person may be suddenly seized with symptoms of severe collapse, ending in a few hours in death. The pancreas and the subperitoneal tissue round it are found infiltrated with blood, which may even extend into the mesentery, the omentum, and the peritoneal region. No cause for this disease is known. The rest of the viscera are usually healthy; fat necrosis is very rare. In almost half the cases there is intense abdominal pain.

FAT NECROSIS.

Contiguous groups of fat cells in the pancreas and in the subperitoneal tissue may undergo necrosis; the fatty acids unite with lime salts, the fat becomes crystalline, and a number of opaque white or yellowish, rather hard patches, usually varying in size between a pin's head and a split pea, and raised slightly above the surface, are seen. They are liable to be mistaken for tubercles or nodules of new growth, and in rare instances have been as large as a hen's egg. These opaque masses melt on heating, stain with osmic acid, and under the microscope seem as it were set among normal cells, with very little inflammatory reaction around them. Fat necrosis is far more common in the peritoneum than elsewhere; the next most frequent seat is probably the pancreas, but it has been described in the subpleural, subpericardial, and subcutaneous fat, and in the marrow of bones. In the peritoneum it is usually in the neighbourhood of the pancreas, and it is found most frequently in association with disease of that region—especially hæmorrhagic pancreatitis. It has been seen, too, in peritonitis, either chronic or acute, and in various other conditions. Often the pancreas is distinctly stated to be healthy. Pancreatic juice can cause necrosis of fat, but the origin of fat necrosis is not properly understood.

W. HALE WHITE.

DISEASES OF THE PERITONEUM.

INTRODUCTORY.

THE abdominal cavity, as it is termed, is in health one in name only—a mere potential cavity. When the potential becomes actual, disease is present. Normally the surfaces, lined by peritoneal serous membrane, are closely pressed together throughout their entire extent; only a small quantity of serous fluid, secreted by some of the endothelial lining cells and reabsorbed by others, intervening. This serous fluid flows in a direction which is chiefly from below upwards. The surface cells over the greater omentum apparently possess the most marked powers of absorption, although the peritoneal membrane as a whole exhibits this faculty to a wonderful degree. May be the peritoneal faculty for rapid removal of fluids from its sac is not so surprising, when the wide expanse of surface presented by it is considered; its total superficies almost equalling that of the body itself. Thus the peritoneum is able not only to secrete fluids, but to reabsorb them, and as a general rule the origin and the symptoms of peritoneal disease are closely related to disturbance of one or other of these functions, except in cases of new growths, malignant and benign, in which the causes are mainly independent of peritoneal secretion and absorption, although many of the symptoms exhibited have their origin in disturbance of these functions. The causes of diseases of the peritoneum are appended in the table on p. 821.

Throughout this article use is made of data derived from the records of the Edinburgh Royal Infirmary for the nine years from 1891 to the end of 1899—data as yet unpublished. In these statistics, attacks of peritonitis consequent upon surgical operations, and cases of pelvic perimetritis and peritonitis in the gynæcological wards, are ignored. Of 72,375 patients treated, 10,411, or 14·3 per cent., suffered from some morbid affection of the digestive system; 1179—1·62 per cent. of the total cases, and 11·3 per cent. of those with alimentary disease—were victims of peritoneal disorders. In Table II. (p. 823) the results of the analysis of these cases are shown in terms of sex and age. The figures tell their own tale.

PERITONITIS.

ACUTE PERITONITIS.

An acute inflammatory condition of the serous membrane lining the peritoneal cavity; primary or secondary in nature; general or local in character.

Etiology.—Acute simple peritonitis (so-called idiopathic peritonitis).—This is an acute inflammation of the peritoneum occurring apart from evident organic lesion. It is a matter of grave doubt whether inflammatory affections of the peritoneal membrane can ever develop wholly independent of concrete external influences. It is true that cases of acute and chronic peritonitis often occur to which it is impossible to assign any direct cause, or, after death, to detect any gross lesion accountable for them. The peritoneal membrane possesses a remarkable facility for the removal and neutralisation of toxic bodies, mainly due, in all probability, to its great power of rapid absorption, and in a lesser degree, perhaps, to a certain

bactericidal property which has been ascribed by many to the secretion of its lining cells. It is a fact worthy of consideration in relation to peritoneal diseases, that the endothelial cells covering the walls of the sac are constantly secreting fluid into a theoretical cavity—a fluid which is as constantly being absorbed again through the membrane. Both the secretion and the absorption of fluid are in great part physiological processes, dependent for their normal pursuance upon the healthy condition of the endothelial cells forming the serous coat. Whenever the normal activity of these cells is altered, their healthy tone diminished, or their vitality destroyed, the processes of secretion and absorption are modified. Decreased power of absorption is of greater influence in causing abnormal disturbance than increased secretion alone. The importance attaching to unimpeded peritoneal absorption is explained by the fact that toxic substances present in the peritoneal fluid are rapidly conveyed to the under liver, to be rendered innocuous in the cells of that great defensive organ of the body under normal conditions.

In idiopathic peritonitis, chills, traumatism without the actual wounding of the membrane, constitutional diseases such as gout and rheumatism, debilitating diseases, chronic kidney disease, profound or pernicious anæmia, and diabetes, are credited with a greater or less share in causation. A point of weight in this connection is supplied by the positive evidence of various observers as to the permeability of the intestinal mucous membrane and its outer coverings, including the peritoneal coat, to various bacterial forms with or without macroscopic lesion; the possibility of invasion of the sac by bacteria circulating in the blood; and the much more facile intrusion of chemical poisons, alkaloids, ptomaines, or leucomaines, through its walls. Some authorities maintain that bacteria are able to pass through the intestinal walls and reach the peritoneal cavity, even although these are perfectly healthy; while others again are of opinion that this is impossible unless there be some peritoneal lesion present. Whichever side the truth lies on, it is notorious that local abscesses, extraperitoneal, adjacent to, but having no direct communication with the lumen of, the bowels, are invariably fœtid and contain organismal forms which have undoubtedly come from the contents of the gut. In appendicitic and perityphlitic intraperitoneal abscesses, with no perforation of the bowel, the pus is generally swarming with other forms, in addition to those micro-organisms normally found in suppuration.

It may be stated, however, as a general rule, that the passage into the peritoneum of bacteria from the bowel cannot *per se* cause an attack of peritonitis, unless they be present in excessive numbers (in which case some gross lesion of the intestinal wall is probably present), except where there is a hindrance to absorption or the coincident presence of an excess of irritating and poisonous toxines. The peritoneum is quite able to deal with any bacteria which may manage to penetrate the healthy intestinal coverings, even if it has to strictly confine their action, and, by building a boundary wall, protecting the major portion of the sac, permit of a purely local inflammation pursuing a local course. But should there be a loss of tone over a portion of its visceral substance, accompanied, it may be, with reflex disturbance of varied, while discrete, causation, in the protoplasmic activities of the endothelial cells, bacteria may be able to gain entrance in such large numbers, and the peritoneal membrane be so much affected as to be unable to deal with them, that even without any gross lesion inflammation may be set up. Especially would this be the case if

abnormal processes in the intestinal contents coexisted, from stasis, or putrefactive fermentation with absorption of poisonous toxines.

To sum up. Cases of acute idiopathic peritonitis are probably the result of some interference with the bactericidal power of the peritoneal sac, normally exercised against the bacteria derived from the bowel, lowered vitality of the endothelial cells, such as follows chills or trauma, and accompanies constitutional affections and general debility.

Acute secondary peritonitis (acute bacterial peritonitis).—This is an acute inflammation of the peritoneum, following invasion by, or extension of, infective and irritant matter, either diffuse or localised, with or without suppuration.

Acute secondary peritonitis arises by extension from acute inflammatory processes affecting organs or tissues immediately adjacent to the peritoneal membrane, by direct contact with infection after perforation of the gut, from intrusion of the contents of an abscess, from the poison of acute general diseases, or by local development of tubercle bacilli. Those cases which are caused by extension from adjacent inflammatory foci differ from idiopathic forms, if the etiological factors given above are accepted, only in degree, not in nature. Acute inflammation of the intestinal wall, such as is common in the protean forms of intestinal obstruction, in strangulation of a hernia, volvulus, intussusception, intraperitoneal constriction, or appendicitic occlusion, may be followed by acute peritonitis, although no actual rupture of the gut has occurred. Whenever perforation of the gastric or intestinal wall leads to entrance of the contents of these organs into the peritoneal sac, bacterial infection necessarily results, usually in irresistible strength. Should the inflammation preceding perforation have induced a local condition of peritonitis by extension sufficient to cause the formation of circumscribing adhesions, the peritonitis following perforation may be rigidly localised. If not, the resulting attack is general. When abscesses burst and discharge their contents into the peritoneal cavity, the type of peritonitic inflammation set up varies with their nature and the amount evacuated. Pus in the pericæcal and appendicular regions always contains other organisms in addition to pyogenic forms.

Perforation of the wall of the stomach or bowel, with escape of their contents into the peritoneal sac; obstruction and strangulation of some portion of the gut, from hernia, constriction, volvulus, and other causes; appendicitis, with or without rupture or gangrene; inflammatory affections of the pelvic organs, particularly in females—such are most frequently the exciting causes of acute secondary peritonitis. When the result of rupture of an abscess situated close to the peritoneal coverings, with discharge of pus into the cavity, a diffuse form of suppurative peritonitis may be present, or, if inflammatory changes in the immediate neighbourhood of the abscess induce formation of peritoneal adhesions before rupture, be strictly localised. Acute suppurative peritonitis, however, often occurs without actual rupture of an abscess; generally in such cases being localised. The common perityphlitic and appendicitic abscesses, originating from passage of organisms through acutely inflamed coats of the bowel, form well-known instances of this.

The acute forms of peritonitis occasionally met with in cancerous, tuberculous, and hydatid infections will be discussed below. Of 355 cases of acute secondary peritonitis, collected by me from the records of the Edinburgh Royal Infirmary from 1892 to 1899, 183 were male, 172 female. In

males, lesions of the appendix and neighbouring tissues were by far the most frequent, followed by ulceration of the intestine and then by intestinal obstruction. Gastric ulcer, on the other hand, occupied the first place among the females, appendicitic disease second, closely followed by obstruction of the bowel. Among the females, again, pelvic diseases were answerable for almost as large a proportion as intestinal obstruction in males. A greater proportion of cases originated from gastric cancer in males than in females, and the converse in connection with intestinal cancer.

Morbid anatomy.—The peritoneal coats in acute peritonitis show all the typical changes common to inflammatory processes. The endothelial cells covering the portion affected multiply, enlarge, and often desquamate (Orth). Treatment of the normal peritoneal surface with a solution of nitrate of silver results in the decolorisation of only a few of the endothelial cells; but after even slight artificial irritation during life, a very much larger number of cells become thus discoloured. Delbet regards the cells thus altered as about to desquamate. Wider and wider interspaces also appear between the cells, corresponding to the degree of irritation they are submitted to. The desquamating cells, before their actual shedding, often proliferate, a fact which probably explains the rapidity with which pus sometimes appears in the peritoneal cavity. The underlying connective tissue also is swollen, œdematous; its cells proliferate, and throw out a fibrinous exudation.

The *Bacillus coli communis* is a common inhabitant of abdominal abscesses, along with the pyogenic micrococci. In suppurative peritonitis of puerperal origin the *Streptococcus pyogenes* predominates; after operation, the last-named, along with the *Staphylococcus pyogenes aureus* and *albus*. The gonococcus also has been found in the peritoneum, in cases caused by spread of infection from the female uterine adnexa. In a few instances it is recorded to have reached the peritoneum in the male from the seminal vesicles or spermatic cord.

Flexner has recorded two cases in which the *Micrococcus lanceolatus* was present in the bowel and found in the peritoneal cavity, where it had given rise to acute and fatal peritonitis, although there was no rupture of the bowel. Diplococci of pneumonia have been found in great numbers in the inflamed peritoneal cavity, and the *Amœba coli* identified amongst the thin fibrinous peritoneal exudations of amœbic dysentery (Osler).

Symptoms.—The mode of onset, the area of membrane involved, the nature of the inflammatory process and of the exudate, and the complicatory lesions, vary the incidence and characters of acute peritonitic symptoms. Intense pain, shock, and symptoms of profound collapse usually follow sudden infection of the peritoneum, such as accompanies external wounds, perforation of a gastric ulcer, or rupture of the bowel. Irritation of the local nervous mechanism of the peritoneum may be so severe as reflexly to lead to a rapidly fatal result, not only in cases directly infected by contents from the alimentary canal, but also in traumatic injuries, even without actual wounding of the peritoneum. Occasionally, perforation of an empty viscus is unaccompanied by pain or shock, acute symptoms subsequently arising on the arrival of food-stuffs at the seat of injury. Still more rare are those cases in which the peritoneum appears to be incapable of painful sensations throughout the attack.

The abdominal pain varies in position with the primary site of infection, but generally most acute at or immediately beneath the umbilicus, and felt less intensely over the whole abdomen. If the cause be perforation of the

stomach wall, the pain may be referred to the back or shoulders; if appendicitic or typhlitic, to the umbilical region at first, but later on over the right iliac fossa. Not uncommonly subjective pain is absent as long as perfect rest is maintained in the posture which proves to be the most comfortable and easy.

Vomiting is an early symptom, and a most painful one, because of the strain and pressure put on the inflamed peritoneum. The vomit is often bile stained; during the later stages, it may be composed of pure bile, sometimes of fæcal matter. The bowels are at first inclined to be loose, but shortly become constipated. The constipation is largely due to a paralysis of peristalsis, with stasis of the intestinal contents—a condition facilitating great evolution of gas, and leading to the tympanites which is so marked a feature of most acute peritonitic attacks.

The patient almost invariably assumes the dorsal decubitus, lying on his back with the knees drawn up to lessen the tension of the abdominal walls, his face pinched and drawn, anxious and suffering in expression, a malar flush—in fact the typical "*facies Hippocratica,*" suggestive often of a graver condition than in fact is present.

The respirations are hurried, shallow, and entirely thoracic; the pulse quick, at or over 90 beats per minute; the temperature rarely above 100° F. As the attack progresses the breathing becomes even more superficial; the pulse rate rises to 110 or up to 140 per minute, the beats being sometimes small and "wiry"; the body temperature mounts up to from 103° to 105° F. In some cases, difficult of diagnosis, no rise of temperature may occur, while the pulse gives no special indication.

The tongue at first is moist but white—furred; latterly dry, angrily red, cracked and fissured. The abdomen is distended, its walls rigid, resenting change of form or position. If the walls are thin, the forms of intestinal coils blown up with gas may be traced on the surface. A tympanitic percussion note may be obtained over the greater portion of the abdomen, obscuring the splenic dulness, and partially obliterating the hepatic dull area, often to outside of the mammary line. Where gases have escaped into the sac along with the contents of the stomach or bowel, a condition known as pneumo-peritoneum, the liver dulness may be almost wholly obscured. When the tympanites is great the diaphragm is pushed upwards, the heart displaced, and respiration embarrassed. The earlier rigidity of the abdominal walls may be succeeded by relaxation, accompanied by great tumescence and distension.

Some effusion of fluid is usual in acute peritonitis; the amount is seldom very large, and is often confined to one spot by adhesions. Occasionally peritonitic friction may be heard over the abdomen in acute, but much less often than in chronic cases.

Diagnosis.—As a rule the diagnosis of acute peritonitis is attended with no great difficulty. The antecedent history of some disease or injury of the alimentary canal conducive to rupture or perforation of the wall, the sudden onset of the attack, the local and general symptoms; above all, the rigidity of the abdominal wall and the characteristic decubitus assumed, serve to indicate the nature of the disease. In idiopathic cases, the conjunction of some debilitating disease with the classical symptoms of acute peritoneal inflammation, a history of exposure or local contusion along with some constitutional ailment or intestinal error, signify the condition present. The thoracic type of breathing, the rapid, "wiry" pulse, and the facial expression, aid in diagnosis.

Prognosis.—Acute idiopathic peritonitis is very fatal if a complication of chronic disease of other organs. In those cases in which it occurs without apparent cause or complication, the prognosis depends upon the general condition of health of the individual attacked. As a rule, recovery results without surgical interference or may follow operation; but where prolonged constipation or intestinal dyspepsia, with acute intoxication, has previously existed, it may be rapidly fatal.

The earlier surgical measures are adopted after the diagnosis of acute peritonitis has been made, the more favourable the prognosis. The mortality after such operations, and solely due to them, is so small under careful conditions, that it may be disregarded when the chance of recovery from the disease is considered, and the high mortality caused by the disease itself, with or without operation, has been discounted.

Treatment.—It is hardly too much to say that the correct treatment of acute peritonitis, whatever it arise from, lies in calling in a surgeon, and the performance by him of abdominal section. Whether the operation be undertaken for exploration only, or be remedial in aim, the risks attendant upon the disease itself far outweigh those of antiseptic laparotomy; the chances of benefit from surgical measures exceed those derivable from purely medicinal treatment. The details of the operations appropriate under various circumstances relate rather to surgery than to medicine, and can scarcely be entered upon here. One point which has not received as much attention as it merits, may be mentioned—the valuable assistance the physician can render the surgeon in the preparation of the patient for operation, not in minor details connected with the state of the bowels or the ingestion of food, but in removing or lessening nervous disturbance naturally aroused by the thought of the coming operation, and in strengthening the heart, generally weakened both by reflex influences and by the actual disease. Co-operation between physician and surgeon before and after abdominal operations, the physician assisting the surgeon through his previous knowledge of the patient's bodily health and idiosyncrasies, is most desirable; early recognition of the surgical nature of all peritonitic lesions, incumbent on the physician; readiness to operate unless clearly contra-indicated, proper for the surgeon.

Where the peritonitis is suppurative in form, and especially if localised, prompt operative interference is obligatory. No delay is permissible here. The removal of purulent exudations may possibly effect a cure; the opening of a localised peritoneal abscess almost invariably does so, while every minute lost increases the risk of rupture of the adhesions forming part of its wall.

The medicinal treatment of acute peritonitis, widely employed and recommended before operative procedures were rendered feasible by the introduction of antiseptic surgery, and still utilised by some, is founded on two diametrically opposed pharmacological actions. Thus some authorities advocate the administration of purgatives; others the exhibition of drugs, especially of opium, able to arrest the intestinal peristalsis. The administration of opium preparations or of morphine has undoubtedly a marvellous effect in subduing pain and discomfort in acute peritonitis, and sometimes even appears to arrest the progress of the inflammation. In most cases, however, the arrest of peristalsis established tends to exaggerate intestinal stasis and fermentation, and to increase the toxæmia present. In the so-called idiopathic cases especially, opium and its derivatives may render the source of infection more potent.

The exhibition of purgatives in acute peritonitis only applies to cases in which no perforation of the gut has occurred. In simple cases, without any gross peritoneal lesion, where absorption of bacteria or toxines from the bowel forms the principal source of infection, bland purgatives given early may abort an attack by removing irritating scybala or fermenting contents from the bowel. If opium be used it should be given in large doses, sufficient to place the patient thoroughly under the influence of the drug, when the absence of intestinal movements and the abolition of painful sensations lessen the irritation of the peritoneum and inhibit the abnormal stimuli reflexly produced by the local nerve fibrils. Bland aperients, castor-oil for preference, combined with small doses of opium, to prevent any excessive peristalsis, may be given early in an attack. This combination generally produces one or two soft motions, without causing pain. In all those cases which are the result of local inflammation in the wall of the bowel, owing to fæcal stasis or impaction, where abnormal numbers of bacteria are enabled to gain the peritoneal cavity, and peritoneal absorption, may be, is diminished, and in which absorption of intra-intestinal bacterial toxines is increased, an early evacuation of the bowel, provided the means used to this end cause little irritation, removes the primary source of infection, and may suffice to quell it; the peritoneum being capable of dealing with the inflammatory condition affecting it, when further accession of toxic agents is prevented.

The local application of ice to the abdomen often soothes pain and relieves distressing symptoms. Heat acts in much the same way, but is not so suitable owing to its tendency to encourage suppuration while relieving pain. Counter-irritation is seldom of any avail, unless the peritonitis be very local in character, and independent of gross lesions. The ascitic fluid present in acute peritonitis rarely reaches a point necessitating aspiration; in fatal cases it usually persists to the end; in others is generally absorbed during the process of recovery, or becomes larger as acute attacks pass into chronic forms.

Should the tympanites become so pronounced as to threaten life by interference with the actions of thoracic viscera, a trocar or cannula plunged into a distended coil of the bowel will allow the escape of some of the gas. The great distension of the bowel and the increased pressure within the abdominal cavity render the entrance of a trocar a matter of much greater ease than when the intestines are flaccid and freely movable within it.

The diet in acute peritonitis should be mainly confined to milk, raw or boiled, and in small quantities at a time; diluted with water, or soda-water, or peptonised. Vegetable substances must be eschewed; meats well cooked, finely divided or thoroughly masticated, and in small amounts, do no harm; meat extracts are allowable. Stimulants are indicated in some cases, contra-indicated in others. The food given should be mainly in fluid form—milk, predigested or raw, meat extracts, egg-flip with whisky, brandy, or champagne; but nothing in large amounts at one time, always "little and often." Hot water, however, taken as hot as can be swallowed without pain, and in considerable bulk, should it be retained, passes into the bowel undiminished in quantity, and often aids in allaying peristaltic paralysis and flatulent distension, while exercising a beneficial effect upon the peritoneum. The almost invariable accompaniment of acute peritonitis—evolution of large quantities of gas within the bowel—gives rise to very distressing symptoms, but may be mitigated by the

method just mentioned, or by the careful introduction of a soft indiarubber tube per rectum as high up the large bowel as possible, irrigation of the bowel with water at the body temperature, and by maintenance of the tube afterwards in position to allow of the expulsion of gas; endeavouring as far as possible by change of posture to facilitate its passage from the colon. Frequently, if the patient be propped up lying upon his left side, after irrigation has been performed, passage of gas from the small intestine into the large follows the removal of the latter's contents; then a change on to the right side tends to pass the gas on towards the open end of the tube, whence without.

Chronic Peritonitis.

Etiology and morbid anatomy.—Chronic inflammation of the peritoneal serous and sub-serous coats, generally characterised by the formation of adventitious fibrous tissue, often by the collection of fluid in the peritoneal cavity.

Primary chronic peritonitis.—It has already been argued that the so-called acute idiopathic peritonitis is caused most probably by incursions of bacterial agents or poisonous toxines, without visible solution of continuity of the lining membrane of the peritoneal cavity. The same arguments apply to the chronic forms of peritonitis provisionally classed under a similar heading. Cases of chronic simple peritonitis belong to two different types—the local adhesive and the proliferative.

Chronic local peritonitic adhesions are very common, frequently give rise to no morbid symptoms of import during life—generally, indeed, are just discovered on autopsy—particularly affect the splenic and hepatic regions, but may occur in any part, and between any two opposing areas of peritoneum, and appear apart from any previous attack of acute peritonitis. The manner in which the peritoneal membrane manufactures those adhesions is a disputed question. Some authorities regard the production and exudation of lymph as the work of the connective tissue cells, situated immediately beneath the endothelial layer, whenever the cells of the latter have suffered loss of vitality, or have been actually removed. By this production of lymph the subjacent cells, deprived of their natural line of defence, or left with but a weakened bulwark, endeavour to lessen the irritation caused by contact with and friction from other peritoneal surfaces, continuously kept in motion by peristaltic contractions, by securing greater fixity of position, and abolishing the possibility of injury from attrition. Others, again, regard local endothelial loss or decay and the production of lymph as contemporaneous, and the result of one and the same cause.

Whichever of these views represents the truth, or it lie between, or outside them, it may be said with certainty that chronic adhesions can scarcely be initiated *in loco*, but can only result from some actual irritation produced by a poisonous agency within the sac, or in the tissues immediately adjacent to the serous membrane, of moderate virulence, but affecting some special restricted area more or less persistently. The exuded lymph rapidly becomes organised, and forms a fibrous connection between two peritoneal surfaces. Adhesions which connect one coil of the small gut to another are usually short, but those in other parts often are stretched out into definite fibrous bands in cases of long standing.

Very probably, in acute attacks of enteritis and gastro-enteritis, excessive intestinal fermentation, and in cases of chronic constipation, in

all of which greater numbers of bacteria, and larger amounts of toxines penetrate the intestinal mucous membrane, and gain access to the peritoneal membrane and cavity, areas of endothelial insufficiency occur, leading to lymph formation; the symptoms of acute peritonitis persisting after subsidence of the enteritic attack, owing to diminished power of checking bacterial invaders where the serous layer is weakened.

Chronic proliferative peritonitis, even better called *peritoneal cirrhosis;* and in many cases, *hypertrophic peritoneal cirrhosis.*—In this condition the peritoneal membrane, in all its layers and usually over its entire surface, is thickened and hardened. Its serous surface shows opaquely white. The thickening is not uniform in degree; in some places it is greater than in others. Adhesions are seldom a prominent feature. Local forms have been separately described under the names of chronic perihepatitis and chronic perisplenitis, in which the peritoneal capsule of the liver and spleen respectively are thickened, sometimes enormously. A depth of as much as half an inch has been recorded in such cases. In most instances the increase in thickness of, and hypertrophy of connective tissue elements in, the capsules of these organs is directly connected with cirrhotic changes in the substance of the glands.

The thickening of the omental coats is usually marked, and is commonly followed by a rolling up of this portion of the peritoneum upon itself, and the presence of a resistant mass lying transversely across the abdomen immediately below the stomach, and above or over the transverse colon, and readily discovered on palpation. Again, the mesentery may be so shortened and contracted by this hypertrophy of its tissues that the intestinal coils are closely drawn together, and may even appear as a ball of no great size in the centre of the abdomen.

Secondary chronic peritonitis.— This may be a sequel of acute peritonitis, diffuse adhesive peritonitis.—Often after apparent recovery from an attack of acute peritonitis, obscure and indefinite symptoms of abdominal unrest persist, or may appear at some period or other afterwards. Their origin is not far to seek. The history of a former acute attack will point to their causation. During the course of every acute attack of peritonitis a certain quantity of inflammatory exudation is produced by the peritoneal cells, varying in degree with the nature of each attack. The lymph thus exuded may or may not become organised, and in course of time form fibrous adhesions. Generally speaking, the inflammatory adhesions of acute peritonitis are many but weak, matting the intestines together, joining them with the omentum, and connecting them with the parietal surface. When these adhesions become more firm and fibrous at a later date, they naturally are liable to interfere with the peristaltic movements of the bowel, and prevent freedom in change of site or bulk on the part of the viscera. Irregularity of bowel function follows, dragging sensations variously located may occur, and intestinal flatulent colic readily produced, owing to hindered motility of the coils of the gut.

Symptoms.—The symptoms of chronic peritonitis are capricious. The only one which can be termed constant is the presence of fluid in the abdominal cavity. There may be no sign of constitutional disturbance, no loss of flesh, or of strength; or the patient may become emaciated, pale, and dyspeptic. Fever is rare, pain and tenderness inconstant. The abdomen, however, is enlarged, distended, often enormously; and yields all the signs and indications of the presence of free fluid within it. The degree of enlargement usually increases gradually through the course of

some months, now and then of as many weeks; often exhibiting variations in rate of increase from time to time, or even some decrease in actual bulk, following and followed by extension. In all forms of chronic peritonitis a friction rub may generally be detected over the upper part of the abdomen, caused by contact between adhesions.

After disappearance of the fluid, by absorption or after aspiration, masses of irregular shape may be palpated in the abdomen, consisting of peritoneal thickenings, areas surrounded by dense adhesions, or of a drawing together of the intestines by reason of shortening of the mesentery.

Treatment.—Medicinally, tonics, iron, arsenic, quinine, and strychnine; hydragogue cathartics, especially salines; and diuretics are indicated; along with light nourishing foods. If under such measures the fluid shows no inclination to diminish, aspiration gives the most satisfactory results; in several cases has been followed by cure. After disappearance of the fluid, gentle abdominal massage may prove of service in lessening the discomfort due to the presence of adhesions, rendering them less rigid, and aiding the intestinal freedom of movement.

TUBERCULOUS PERITONITIS.

Tuberculous invasion of the peritoneum may either be acute or chronic, localised or general, primary or secondary. In the rare cases which may be termed primary, the peritoneal membrane is the seat of active tuberculous processes, generally displayed in the form of tuberculous nodules spread over its surface; when acute, usually of small size but in enormous numbers; when chronic, fewer and larger, and perhaps more often localised in one part. In secondary cases, in which invasion of the peritoneum follows directly upon infection from previous tuberculous processes in other tissues, their distribution and their intensity depend upon the virulence of the infective poison. The resulting invasion may be purely local and circumscribed, and of a chronic, inactive nature, or may rapidly spread over all the peritoneal surface in an acute form. The acute forms are rarely met with except in cases of general miliary tuberculosis.

Etiology.—Although most frequently met with in the young, tuberculous peritonitis often occurs in adults—oftener, perhaps, than is commonly supposed. It is usually asserted that males are more often attacked than females, but the records of the Edinburgh Royal Infirmary show practically an equality between the sexes—144 to 142; although under the age of 9, males, and above 19, females, are distinctly the more numerous. Osler noted in the statistics of laparotomies for tuberculous peritonitis collected by him, that females and males were as 2 to 3. The same authority, analysing 357 cases collected from the literature of the subject, found the ages of 346 to be as shown in the table.

The proportion of cases recorded under the several ten-year periods in the two series differs radically. In the Edinburgh series the numbers registered during the first two decades of life are far above Osler's corresponding figures; while the converse holds true for all the following periods. Thus the number treated in Edinburgh between the ages of 10 and 19 formed 45 per cent. of the total; under 9 years, 22·7 per cent.; Osler's figures for these decades yielding only 21·67 per cent. and 7·8 per cent. respectively. The large number of cases shown in Osler's statistics over the age of 40 is surprising. There was a marked predominance of

cases in males below the age of 10, an equality in number between the two sexes from 10 to 20, and thereafter a larger number of female cases.

The statistics of operations for tuberculous peritonitis hitherto gives females a large majority; those of post-mortem records an equally high proportion in favour of males. Thus Osler, from collected statistics of laparotomies, found the number of female cases to be 131, of males only half, or sixty. König, in a series of 131 operations, records only eleven men against 120 women, or 1 to 11. Among the 286 cases from the Edinburgh Royal Infirmary records, the proportion of males to females in the sixty-eight cases operated upon was much higher—31 to 37. Combining these various figures, out of a total of 390 laparotomies, 288 were female, only 102 male—a proportion of almost three to one.

On the other hand, of 107 post-mortems analysed by Curtis, eighty-nine were on males, eighteen on females. The Edinburgh figures again fail to correspond—nine males to thirteen females.

Tuberculous peritonitis often accompanies pulmonary tuberculosis, frequently along with tuberculous enteritis, and in cases of tabes mesenterica. Tuberculous infection of the abdominal lymphatic glands, especially of those situated in the mesentery, leads frequently to direct peritoneal infection, when a caseous gland ruptures into the sac. In women, direct invasion often proceeds from the Fallopian tubes; in men, extension of tuberculous processes has been noted from the vas deferens. Phillips gives 74 per cent., Pribram 53 per cent., and Sick 65 per cent., as the relative frequency of intestinal infection; the latter according the female pelvic organs with 26 per cent., Osler with from 30 to 40 per cent., Pribram with only 4·8 per cent. out of 165 cases. Osler, from the results of seventeen autopsies, concludes that in five, or 29·4 per cent., the tuberculous condition was truly of primary origin. From observation of 107 autopsies, König records concomitant tubercle of the lungs in 92·5, the pleura in 56·04, the intestine in 74·72, the peritoneal lymphatic glands in 41·09, the spleen in 37·36, the kidneys in 35·49, and the liver and adrenals in each 56 per cent.

Morbid anatomy.—In the ordinary chronic variety, groups of tuberculous nodules coalesce to form larger masses, of different sizes, usually flattened in shape, and becoming caseous. Adhesions may stretch between the various peritoneal surfaces, which in turn are frequently thickened. In the fibroid form the nodules are harder and not aggregated in masses, while the serous surfaces are matted together by numerous fibrous adhesions. The exudation in the first form may be purulent or sero-purulent; in the second it is seldom large in amount, often absent.

Symptoms.—Chronic tuberculous peritonitis not infrequently gives rise to few symptoms of moment for a considerable period of time after the actual commencement of the disease. It may indeed be latent, and only discovered during an operation or post-mortem. The more gradual the onset, the longer the course of the disease. The commoner symptoms include abdominal pain, slight or severe, circumscribed or diffuse, with or without tenderness; enlargement of the abdomen, general or localised; and pyrexia of a cachectic type, seldom intense, often in fact replaced by, or alternating with, periods of subnormal temperature. The abdominal swelling may be caused by collection of fluid in the peritoneal sac, by tympanites, or by both of these factors. The fluid, if in large amount, may support the intestinal coils on its surface, provided that they are not bound down by adhesions; and thus afford a tympanitic percussion note, varying in site and area with the decubitus, over the position of the float-

ing bowel, surrounded by a dull region similarly changing in size and place. When, as often happens, the exudate is encapsulated by peritoneal adhesions, the presence of cystic tumours may be suggested. Distension of portions of the bowel with gas, in connection with such localised effusions and adhesions, may appear as elastic, rounded tumours, which do not show changes in site on altering the position of the body. As the formation of adhesions proceeds as a rule *pari passu* with the course of the disease, symptoms of disturbance of digestion, from their interference with the mobility and motility of the gut, are more and more liable to appear —loss of appetite, dyspepsia, reflex nausea, diarrhœa, or constipation. Obstruction of the bowel may be a result. In addition, save in the latent cases, increasing emaciation and debility mark the progress of the disease.

An elongated, sausage-like, firm mass, lying across the upper part of the abdomen, easily palpable, usually dull on percussion, but occasionally resonant owing to interposition of a coil of intestine, sometimes found in the right iliac region, denotes the omentum, thickened, contracted, and rolled on itself. Met with in cancer and chronic cirrhosis of the peritoneum, it is more common in tuberculous peritonitis.

Diagnosis.—Perhaps the difficulties attendant upon the diagnosis of chronic tuberculous peritonitis may be correctly said to increase with the age of the patient. In the young it is seldom a difficult problem to decide upon. In patients of greater age, especially in women, the large number of laparotomies undertaken for the removal of supposititious ovarian cysts, but resulting in discovery of tuberculous peritonitis, renders it apparent how readily mistakes can be made.

A careful consideration of all the etiological factors offers the most valuable evidence. Non-tuberculous chronic peritonitis often simulates the tuberculous form very closely. A history of antecedent tubercle or of pleurisy with effusion may point out its true nature. The general absence of fever with ovarian tumours, and their less speedy enlargement, aid in distinguishing between them and this disease ; while ascites caused by other agencies may be eliminated by determination of the true underlying lesion.

Prognosis must always be guarded. Osler gives 25 per cent. as the proportion of recoveries. Some authorities regard cases with exudation as of more favourable augury than those without ; others hold the converse to be correct. The prognosis is undoubtedly better in the young than in adults, but no case can be regarded as other than serious before operative interference. After operation it is generally readily determined whether a hopeful result is possible or not.

Treatment.—In treating cases of tuberculous peritonitis, much depends upon the stage to which the disease has advanced, and upon the virulence of the attack. In chronic and subacute tuberculous peritonitis, whether general or local, treatment in the earlier stages should consist in rich dieting, especially in fats, in avoidance of confined atmospheres, and in enjoyment of open air life as far as possible. Iodoform, internally, often is of benefit; and mercurial inunction may be employed. At what stage operative interference can reasonably be resorted to is a question which is difficult to answer; when performed in cases of considerable severity, laparotomy and thorough flushing of the abdominal cavity have often been followed by the best results. Logically, the earlier such treatment is adopted the better the result. But so many cases recover under medicinal

and dietetic treatment, that the risk attendant upon all abdominal operations can scarcely be properly encountered when the disease is still of early stage. Operative interference is scarcely to be recommended where tuberculous processes in other organs coexist. If the origin of the tuberculous peritonitis proceeds by direct infection from one or other organ, or some adjacent tissue, and the fact be clearly recognised, laparotomy with the view of removing the primary source should be at once performed; but if the source be doubtful, while possibly of such a nature, an exploratory operation is more to be commended than reprehensible.

No method of treatment is of much avail in acute tuberculous peritonitic attacks. These are usually local manifestations of a general infection; occasionally, however, confined to the peritoneum. In both instances the potency and degree of virulency possessed by the causal bacilli render remedial measures useless.

If the tuberculous process be localised, and by the reparative actions of nature confined within efficient barriers, evacuation of the contents and irrigation of the cavity generally succeed in preventing further mischief. When phthisis pulmonum coexists, if the rational methods of combating consumption are employed, food taken often and to some degree in excess, should it be simple and easy of assimilation, along with a constant existence in fresh and uncontaminated air, the peritoneal affection will usually be cured before that of the lung; it forms, as a rule, the outcome of a more attenuated virus, and is generally more amenable to treatment than the pulmonary lesion.

TABES MESENTERICA.

The term tabes mesenterica is applied to tuberculous infection of the mesenteric glands, and by many is regarded as distinct from tuberculous peritonitis. A number of authorities, however, do not differentiate between them, but group them under tuberculous peritonitis. In truth, tabes mesenterica often is accompanied by tuberculous peritonitis; tuberculous peritonitis by tabes mesenterica; but, on the other hand, examples are certainly met with in children in which no symptoms of peritoneal infection can be traced, although the mesenteric glands are undoubtedly affected.

Etiology.—Tabes mesenterica is a disease of early life, and in nature closely resembles the processes so commonly met with in tuberculous affections of superficial lymphatic glands at a similar age. The causal agents of infection reach the glands in most cases from the intestine, and apparently may often do so apart from active tuberculous disease in the bowel itself. Lymphatic glands throughout the body are peculiarly open to tuberculous infection of a non-virulent type, when all the other tissues are strong enough to inhibit growth of the *Bacillus tuberculosis*. So, in the abdomen, tuberculosis of the peritoneal glands, uncomplicated by affection of other organs, progresses slowly, does not tend to spread further, to any great extent, unless one of the glands ruptures into the peritoneal sac, and is very amenable to appropriate treatment.

Symptoms.—If the attention be drawn to a child suffering from tabes mesenterica, at an early stage, the only objective symptoms noticeable consist in a slight enlargement of the abdomen; subjectively, interrogation will probably extract the fact that the little patient has for some time before shown a listlessness, disinclination to play, and a preference for sitting over the fire, foreign to earlier habits and to those natural to youth.

The appetite does not diminish, may indeed increase, but the child loses flesh while the abdomen enlarges. Palpation performed firmly will reveal the presence of a sense of resistance from doughy masses collected towards the posterior wall of the abdomen. If the condition be allowed to advance, the abdominal swelling increases, emaciation of the rest of the body rapidly becomes more pronounced, diarrhœa sets in, and death follows from exhaustion. As medical officer of a large boarding-school, in which children of the poorer classes are admitted when about 7 years of age, the writer has had many opportunities of observing examples of abdominal tuberculosis under very favourable circumstances,—in a number of cases in which sources of error from presence of tympanites or ascites could be clearly eliminated; in which palpation and percussion of the abdomen revealed the presence of abnormal masses, painless, soft, amorphous, hardly possible the result of lymphatic obstruction of chyle; in which the body weight decreased, the temperament altered, the appetite increased, and, in some, diarrhœa occurred; and in which fresh air, fats, increased nutriment, and iodoform speedily occasioned decrease of the abdominal masses, with increase of the body generally in bulk and vigour, followed by restoration to health.

Treatment.—Uncomplicated cases of tabes mesenterica respond to appropriate treatment almost more readily than any other tuberculous condition. Secondary infections appear to be rare until the latest stages are reached. As insufficiency of diet seems to be the cardinal point, improved food, cod-liver oil, butter or cream, fresh air and exercise, are essential in treatment. As to drugs, for cod-liver oil is a food not a drug, the writer has obtained more good by the internal administration of iodoform in from 1 to 3 gr. doses twice or thrice a day, than from any other medicine; especially if the patient be allowed to go about, to be outside, to partake of the articles of his ordinary diet in amount sufficient for his needs, adding to it some form of fat in cod-liver oil or cream; but if possible not confined to bed or the sickroom.

As tuberculous affection of the mesenteric glands is closely associated with infection of the peritoneal membrane itself, treatment beneficial in the first acts satisfactorily in the second form, unless the latter be of an acute and virulent type. Inunction of the oleate of mercury through the skin over the anterior abdominal wall is an excellent accessory, or the soluble metallic salts of mercury lately introduced may be used with advantage.

MALIGNANT PERITONITIS.

Etiology and morbid anatomy.—Primary carcinoma of the peritoneum or of the peritoneal lymphatic glands is uncommon. When it does occur it usually resembles primary cancer of the pleura, that is to say, it is an endothelioma. Nodules of unequal size stud more or less closely the peritoneal surface, the layers of which are greatly thickened. Great effusion of fluid into the peritoneal sac often follows, generally along with a deposition of fibrin; the fluid effused frequently containing blood corpuscles and pigment.

Secondary carcinomata of the peritoneum are very common, and either occur by direct extension through continuity of tissue, or are due to introduction through the lymphatic vessels of infective material from without. Colloid or alveolar cancer elsewhere, by reason of its rigid stroma and enlarged cells, is rarely accompanied by peritoneal metastasis

through lymphatic transportation, but frequently primary growths extending through the walls of the stomach or the bowel infect and penetrate the peritoneal coats. Indeed, no secondary form of cancer so commonly causes secondary peritoneal growths as the colloid variety when present in the stomach or bowel. By rupture of a malignant ovarian cyst, direct cancerous infection of the peritoneum may be caused; the variety of carcinomatous growth thus produced corresponding to the form present in the original tumour, generally medullary or colloid in nature. Among other forms of secondary cancer attacking the peritoneum, scirrhus is met with, proceeding by actual infiltration of tissue from adjacent growths, or by way of the lymphatics; and, similarly, cylinder-celled epitheliomata. Although secondary cancer of the peritoneum may arise from primary growths in any of the abdominal and pelvic viscera, and may accompany others of more distant location, it is most frequently engendered by cancerous disease of the stomach and ovaries.

In connection with the local changes produced, it should be borne in mind that, as already stated, there is a constant passage of fluid in the peritoneal sac, flowing, generally speaking, from below upwards; secreted as well as absorbed by the endothelial cells lining the cavity, those covering the omentum having apparently most to do with absorptive processes. Whenever cancerous material finds its way into the cavity, it is carried along by this current and distributed widely throughout the whole cavity, giving rise to numbers of secondary foci of disease. As is but natural, the cancerous nodules thus developed are as a rule of larger size the nearer they lie to the source of distribution of infective particles; the smaller, the further away from it; not more numerous on the surface directly below, or, although the intraperitoneal current runs from below, up, its flow is insufficiently strong to arrest the action of gravity.

The great omentum, however, probably because it acts as the chief drain of the peritoneal cavity, is often greatly involved; sometimes forming in colloid cancer great bulky masses, in others large tumours, or causing the omentum to become rolled up upon itself, and to assume the shape of a solid mass, lying transversely across the abdomen immediately beneath the lower margin of the stomach, as described above.

The figures given in the table on p. 823 exemplify the much greater tendency to peritoneal malignant disease shown by women, especially between the ages of 40 and 60, than by men. During the earlier years, from 10 to 40, the total figures are equal; between 40 and 60 the males are to the females as 1 to 1·7; from 60 to 80 as 1·00 to 1·11. Again, cases of cancer of the peritoneum generally are much more common among women; of cancer especially affecting the greater omentum, the mesentery, and the abdominal lymphatic glands, more frequent in men.

Sarcoma.—Primary sarcoma of the peritoneum itself is rare; although the retroperitoneal glands not infrequently are invaded by primary lympho-sarcomata, which may attain to large dimensions, and displace many of the abdominal organs by their growth. The cylindroma usually develop in the subserous peritoneal coat, often reaching to some size without invasion of the adjoining walls. Lympho-sarcomatous growths may develop in the mesenteric glands, involving in time all adjacent organs and tissues, and among them the peritoneum secondarily. In the Edinburgh statistics, the small number of sarcomatous affections of the peritoneum included renders any separate deduction from their distribution of but slight value; still six of the cases occurred in females, while only two were males.

Forms of hyaline and myxomatous degenerative changes in the peritoneum, usually associated with ovarian cysts, in which the whole serous membrane is coated with a thick layer of hyaline or mucoid material, are closely analogous to the sarcomata.

Symptoms and diagnosis.—In cases of primary cancer, the diagnosis may be attended with some difficulty. Chronic ascites, with progressive emaciation, constitutes the main clinical feature. If the ascites be great, little can be gained from local examination; but, after tapping, resistant nodules may be felt at some part of the abdomen, or the omentum detected lying curled up as a bulky transverse mass below the lower border of the stomach. But, as Osler points out, a very similar mass often occurs in tuberculous and chronic proliferative peritonitis, and therefore is not to be regarded as pathognomonic of cancer.

In cases of secondary invasion, a history of malignant disease elsewhere renders diagnosis easy; the symptoms detailed above directing attention to the peritoneal involvement. The presence of large multiple nodules indicates cancer; in those over middle age more surely than in younger persons, in whom similar nodules may arise from tuberculous peritonitis or tabes mesenterica, though these as a rule are softer to the touch and of less definite shape. In cancer, again, there may be some involvement of the inguinal glands and of the skin round the umbilicus. The characters of the effused fluid in cancer are very similar to those in tuberculous peritonitis, but may contain the large polynucleated cells, or the cell-groups typical of cancer.

When the abdomen is the seat of large colloid cancerous tumours, and distended by a gelatinous, semi-solid material, the clinical symptoms are very different; the abdominal walls are tense, firm, and elastic; over the greater part dull on percussion; no signs of fluctuation can be obtained, nor change in the area of dulness on alteration of decubitus.

Nodular echinococcal cysts in the peritoneum sometimes produce symptoms so closely akin to those of cancer, that a definite diagnosis may be impossible.

Treatment.—In all cases of cancer of the peritoneum, treatment can only palliate, can never cure. Symptomatic measures for relief of pain, for lessening discomfort from intestinal disturbances, for maintenance of strength by proper food, and for the reduction of abdominal pressure by removal of ascitic fluid, are indicated. Instances, indeed, have been recorded in which aspiration of fluid, followed by introduction of medicinal substances into the peritoneal sac, brought about an apparent cure; but such cases must be looked upon with suspicion. Sarcomata of the peritoneal lymphatic glands, when recognised at an early stage, and surgically explored, have before now been successfully removed—but only on very rare occasions.

SYPHILITIC PERITONITIS.

Syphilitic invasion of the peritoneum is rarely met with, except in instances of perihepatitis in which syphilitic changes have extended from the liver. One case of syphilitic enlargement of the peritoneal lymphatic glands is included in the series of 1179 peritoneal lesions referred to above. Secondarily, syphilis may lead to attacks of peritonitis by rupture of the waxy coats of the bowel, or from the lessened power these coats have, when in such a condition, of hindering bacterial and toxic invasions.

SIMPLE TUMOURS.

Lipomata occasionally occur, springing from the retroperitoneal fat, or the fat in the mesentery and omentum. Fibromata have been recorded. Hydatid cysts are often found growing in the peritoneal subserous coat. Only sterile and composite cysts develop in this position; multilocular cysts never occur. The most frequent source of infection seems to be the escape of a daughter cyst from a mother cyst in the liver, apart from actual rupture of the latter into the cavity, a disaster rare and generally fatal.

Hydatid cysts of the peritoneum can only be treated by operation. Aspiration and injection of irritants has proved useless. When the abdominal cavity has been opened, the number of cysts present will serve to indicate if their removal be feasible or not. Great care must be taken not to rupture any of the cysts within the abdomen, as their contents are highly infectious, and liable to cause a further crop of new growths.

PERITONEAL FLUIDS AND ASCITES.

Etiology.—The presence of abnormal fluid in the peritoneal sac, caused either by increased transudation, diminished absorption, or by exudation. The peritoneal cavity normally contains a small quantity of fluid which is continuously circulating through it. The serous membrane of the sac has great powers in transudation and absorption. Watery solutions, oils, even bile, are quickly absorbed, and finely divided solids are also readily carried off by the lymphatics. The surface of the great omentum and of the diaphragm appear to be specially concerned with the process of absorption (Coats). Ascites will therefore arise whenever there is marked increase of transudation of fluid from the blood, or lessened power of absorption; or it may be, when both these factors are present. When the fluid collected is the result of mechanical action only, it presents the characters common to simple transudations, when caused by organic lesions of the endothelium lining the cavity, those of exudations.

The physical causes of ascites are either general or local. Among the general causes obstruction to the circulation of the blood in valvular heart disease, weak cardiac action, chronic pulmonary emphysema, and pneumonia rank first; secondly, hydræmic states of the blood, as in chronic nephritis and malaria. More local causes of importance are hepatic obstruction, thrombosis of, and pressure of tumours on, the portal and hepatic veins, and obstruction of the lymphatic vessels or the thoracic duct. The organic lesions giving rise to peritoneal exudations are inflammatory conditions, acute or chronic; tuberculous infection; and malignant growths.

Morbid anatomy.—Where the presence of fluid is independent of actual local disease of the peritoneum, no morbid change in the characters of the serous membrane may develop until the condition has lasted for some time; it becomes later somewhat thickened and opaque. The fluid present may vary in amount from a few ounces up to several gallons. It is generally of a light yellow colour, often with a slight greenish tint; but, especially in cases of hepatic obstruction, may be of a brownish green hue from bile pigments, or ruddy from hæmoglobin derivatives. Clear as a rule, the presence of a barely soluble serum-globulin often renders it

opalescent. The reaction is feebly alkaline or neutral. Its specific gravity varies from 1008 to 1020. Spontaneous clotting is seldom if ever observed. The specific gravity of exudative fluids is usually higher than that in transudation. In the former class, it rarely falls below 1014, almost never below 1012; in the latter, it may be as low as 1008, seldom exceeding 1012, but more apt to reach an abnormally high level than the former is to descend below the average minimum. The mean specific gravity of forty-eight peritoneal fluids of various types, analytical details of which the writer collated from extant records, works out at 1016·7; of the seventeen exudations, at 1018·8; of the twenty-four transudations, at 1013·4; and of four examples of true chylous ascites, at 1024. But it is of importance to remember that these figures are only applicable as means, and that great divergences from them are commonly met with in single specimens of any one of these groups. This fact suggests that the results obtained by examination of individual specimens may be very misleading, unless the possibility of such wide variations occurring be remembered, and all the different circumstances germane to the matter considered with regard to it. The proteid-quotient, as it is termed, or the relation of the serum globulin present in a fluid to the serum albumin —the former taken as equal to 1—is too variable a factor to be of any real assistance for diagnostic purposes; but the means for the value of this factor showed serum-albumin to be proportionally less than serum-globulin in exudations, greater in transudations and chylous ascites. The quantity of fat present in chyliform ascites varies greatly; in those cases which accompany tuberculous and malignant peritoneal diseases, with fatty degeneration of cells cast off by them into the ascitic fluid, it may be considerable; in chyliform transudations, arising from obstruction to the flow of lymph in some of the smaller lymph canals or glands, the amount is generally small; while in true chylous ascites with direct communication between the thoracic duct and the peritoneal cavity, and leakage of the contents of the former, the fat is in greater proportion.

A variety of ascites has been described under the name of "The Ascites of Young Women" (Cruveilhier, Bonilly), and regarded by Cruveilhier as idiopathic, consists in the appearance of ascites without premonitory symptoms in such subjects. On the other hand, Bonilly looks upon these cases as the result of tuberculous affections of the genital organs secondarily invading the peritoneum. The intestines are matted together, and do not show much change of position with change of decubitus. The abdomen anteriorly is flat, but bulges in the flanks. The fluid generally disappears after a variable period.

Bacteriology.—The micro-organisms which have been found in peritoneal fluids do not represent so many separate classes as might have been supposed. The pyogenic micrococci—both strepto- and staphylococci— are of course common in septic forms. The various organisms of almost identical form and character classed under the name of *B. coli communis* are frequent, probably invariable, immigrants in peritonitis following perforation of the alimentary tract, whether localised or diffuse. They must be judged guilty, also, of traversing the bowel coats, and of reaching the peritoneum in many cases of inflammation of the peritoneum with effusion, arising without actual gross lesion, and due to intestinal catarrh.

Quantity of fluid.—The large quantities of ascitic fluid which have been removed from the peritoneum at one sitting are most remarkable; but still

more remarkable are the cases in which, by repeated tappings at short intervals, the quantity of fluid obtained has reached *in toto* to enormous bulk. In one case known to the writer, 4 gals. were removed at the first tapping; and 9½ gals. during the following 130 days, or 13·5 gals. in 131 days, a loss of about 135 lb. in weight. In another case recorded, 640 gals. of fluid were removed from the abdomen of a woman by 151 separate tappings, extending over a space of thirteen years. The total fluid removed represents 6¼ tons in weight, or, supposing the patient's weight to be 9½ stone, 108 times that figure. In these cases the daily increment in peritoneal fluid amounted to about 12 oz. and 21 oz. respectively, containing ¾ and ½ oz. of proteids.

Symptoms.—The signs and symptoms presented by the presence of fluid in the abdominal cavity are influenced by various circumstances. They alter with the amount of fluid present, its environment, the characters of the effusion and the nature of its primary source, and are frequently rendered obscure by reason of the presence of coincident lesions.

When the amount of fluid is but small, it is by no means an easy task to detect its presence, the more so should the fluid be locally impounded. Enlargement of the abdomen, gradually increasing, and showing considerable variations in shape on change of posture, dulness on percussion over the flanks when recumbent, with a resonant note anteriorly, the dull area in the erect posture covering the lower part of the abdomen, the production of the wave of fluctuation, and of the thrill indicative of free fluid in a soft elastic-walled cavity.

Treatment.—The treatment of ascites depends entirely upon a proper appreciation of the cause. There is perhaps no other condition which demands so much care in accuracy of diagnosis. Is it due to hindered circulation of the blood? If so, from what lesion? To altered composition of the blood? From what? To organic affections of the peritoneum? Are these primary or secondary? Whenever circulatory disturbances have been found to be the causal agent, whether the site be in the heart, lungs, kidney, liver, or of a more local nature, the indications for treatment can be briefly stated to be—facilitate the circulation, removing increase of backward, increasing diminished forward pressure, encourage loss of fluid by the emunctories, decrease the bulk of liquids ingested. The details germane to these methods of treatment in each instance need not be enlarged upon here; under cardiac, renal, hepatic, and other headings, full details may be found. In some cases, especially those in which the collection of ascitic fluid is due to a local compression of efferent blood vessels or lymph canals, paracentesis is authoritatively called for, and may have to be repeated at brief intervals for a long period of time. As a rule, the aspiration of ascitic fluid, which is of more general origin, tends to facilitate replacement of the fluid withdrawn. More benefit accrues from the adoption of measures adapted for the removal of fluid from the body *per vias naturales*, and by the decrease of blood pressure thus occasioned, than by violent abstraction of what has been produced by nature in opposition to and by invitation from pathological conditions. In the aspiration of peritoneal fluids, care must always be taken not to remove too great an amount at one time. The abdominal veins are so capacious,—indeed, they are said to be able when fully distended to accommodate all the blood in the body,—that sudden relief of the pressure exerted by ascitic fluids may allow so much blood to collect in them, relaxed in tone as they temporarily must

be from the previous pressure, as to induce syncope or fatal collapse. Often removal of a comparatively small portion of the fluid present, by relieving pressure upon the vessels of the bowel, will initiate absorption of the remainder.

The bladder should be emptied before aspiration, to prevent any chance of injuring it, as full bladders have been tapped under the belief that ascites was present. Full antiseptic and aseptic precautions should be taken, and the trocar introduced at a dependent part, according to the posture of the patient, as the fluid tends to gravitate to the lowest part of the abdominal sac, and the intestinal coils to float on its surface. But the danger of entering the bowel wall is not great, as any one who has endeavoured to pierce such an elastic organ, floating freely in fluid, must have found. When finally withdrawing the cannula, pressure should be exercised upon the abdominal walls to prevent suction of air into the peritoneal cavity; the wound resulting from it being speedily sealed up with cotton-wool and flexile collodion.

When the obstruction to the portal circulation has its seat in the liver, and arises from cirrhotic changes or from cancer, little good can be done by any kind of treatment. The ascitic fluid may be constrained to remain within reasonable bounds by abstraction of fluids, as above, combined with tappings. Here, tapping the abdomen is advisable for the relief of the suffering caused by over-distension, a condition often unavoidable. The ascites which often accompanies chronic forms of nephritis, springs largely from the hydræmic state of the blood, and requires to be treated by methods proper for renal disease, along with those already recommended for other forms.

The peritoneal effusions of pernicious anæmia or leukæmia are seldom susceptible to any kind of treatment save palliative aspiration. Those obscure and doubtful cases of ascites which have been attributed to neurotic vasomotor disturbances, rarely require tapping. Anti-neurasthenic methods of treatment generally succeed in time, while threats of abdominal exploration, perhaps even visible preparations made for performing aspiration, are sometimes remarkably efficacious.

In cases of true chylous ascites, from lesion of the thoracic duct, it might conceivably be possible to reach the seat of injury and close the leak, or, if the ascites be due to local rupture of lymphatics in the mesentery, to ligature them. Lactescent ascites, or *ascites adiposus*, constituting but an unusual variety of other forms, is treated in accordance with its true nature.

The treatment of peritoneal effusions occurring in tuberculous disease and in peritonitis has already been outlined.

TABLE I.—*The Chief Diseases of the Peritoneum, arranged as to Origin.*

I. PERITONITIS.

A. "Idiopathic" or simple.

1. External . . { Contusions. / Chills.
2. Constitutional . { Rheumatism. / Gout. / Debilitating diseases.
3. From adjoining tissues . . } Rupture of sterile cysts.
4. Intestinal ; without solution of continuity, due to { (a) Bacteria. / (b) Toxines.

TABLE I.—Peritonitis—*continued.*

1. Traumatic . . { Wounds. / Operations.

2. Gastro-intestinal . {
(α) Perforation of stomach and bowel . . . {
Gastric ulcer.
Gastric cancer.
Phlegmonous gastritis.
Intestinal ulcer; simple, enteric, tuberculous, dysenteric, and cancerous.
Intestinal acute obstruction.
Appendicitis.
Perforation by foreign bodies.
Purpura.
}
(β) Extension of inflammatory process through walls.
}

3. Hepatic . . {
(α) Abscess of liver.
(β) Cholecystitis; perforation of gall bladder.
(γ) Rupture of hydatid cyst.
}

4. Pancreatic and splenic . . {
(α) Inflammation—acute, hæmorrhagic.
(β) Necrosis.
(γ) Cysts.
}

5. Genito-urinary . {
(α) Inflammation of uterus and adnexa . . { Septic. / Tuberculous. / Gonorrhœal. / Puerperal. }
(β) Ovarian and uterine tumours.
(γ) Cancer of bladder, etc.
}

6. From adjoining tissues . . {
(α) Retroperitoneal abscesses.
(β) Empyema; pyo-pericardium.
(γ) Abscess of lung.
(δ) Erysipelas of parietes.
}

7. Infectious diseases {
(α) Measles.
(β) Scarlatina.
(γ) Variola.
(δ) Influenza.
(ε) Tuberculosis.
(η) Pyæmia, septicæmia . { Streptococcus, staphylococcus, *B. coli communis.* }
}

1. Previous acute attacks. {
(α) Diffuse.
(β) Localised.
}

2. Infectious diseases {
(α) Tubercle }
(β) Syphilis } . . . Diffuse or circumscribed.

3. From adjoining tissues . . {
(α) Fibrous; perihepatitis; perisplenitis . } Cirrhosis of liver and spleen.
(β) Suppurative, localised.
}

4. Chronic inflammation of bowel and appendix. } Diarrhœa; constipation; chronic appendicitis.

5. Chronic auto-intoxication; with peritoneal irritation.

6. Parasites . . {
(α) Echinococcus.
(β) Actinomyces.
(γ) Cysticercus cellulosæ.
(δ) Filaria sanguinis hominis.
}

Left margin labels:

B. Secondary.
   (a) ACUTE.
   (b) CHRONIC.

C. Ascites.
   HYDROPERITONEUM.

1. Inflammatory . {
(α) Acute and chronic peritonitis.
(β) Cancer of peritoneum.
(γ) Tuberculous peritonitis.
}

2. Transudatory . {
(α) Venous congestion and obstruction . . {
Portal thrombosis.
Hepatic cirrhosis and cancer.
Cardiac lesions.
Pulmonary obstruction.
Chronic kidney disease.
}
(β) Hydræmia . . . {
Chronic kidney disease.
Profound anæmia.
Leukæmia.
Malaria.
}
(γ) Obstruction of lymphatics.
}

3. Traumatic . . { Rupture of thoracic duct, or of lymphatics . } Chylous ascites.

4. Unknown . . Without apparent cause in young women and children.

II. NEW GROWTHS.

1. Carcinoma
   - (a) Primary.
   - (b) Secondary
     - 1. By extension.
     - 2. By metastasis.

2. Sarcoma
   - (a) Primary.
   - (b) Secondary
     - 1. To stomach or bowel.
     - 2. To pelvic organs.
     - 3. To liver, pancreas, retroperitoneal glands, etc.

3. Tuberculous mesenteric glands.
4. Hydatid cysts.
5. Benign tumours
   - (a) Cysts, simple and dermoid.
   - (b) Fibroma ; lipoma ; angioma.

III. ABNORMALITIES.

1. Congenital
   - (a) Meckel's diverticulum.
   - (b) Persistent urachus.
   - (c) Inguinal hernia, etc.

2. Acquired
   - (a) Floating kidney
     - Pregnancy.
     - Tight-lacing.
     - Loss of flesh.
   - (b) Gastroptosis.
   - (c) Displaced liver or spleen.
   - (d) Hernial sacs.

TABLE II.—*Analysis of* 1176 *Cases of Peritoneal Disease.*

DISEASES.	Age in Decades. 1-9		10-19		20-29		30-39		40-49		50-59		60-69		70-79		80-90		Totals. M.	F.	Tl.
	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.			
A. Peritonitis—																					
I. Acute Simple	1	..	5	4	8	13	2	3	3	1	..	..	..	1	..	..	..	..	20	21	41
Chronic simple	..	..	2	1	1	3	2	1	1	3	..	1	..	..	..	..	..	..	6	9	15
Proliferation	..	..	1	1	1	1	4	3	3	1	1	..	1	..	..	..	..	..	10	7	17
Adhesions	3	1	4	..	2	2	1	5	2	1	1	2	2	2	..	..	1	..	16	13	29
II. Acute Localised	..	1	1	1	3	3	..	3	..	..	..	1	..	..	..	..	..	..	4	9	13
III. Suppurative—																					
1. General	..	..	..	1	..	1	..	..	..	3	..	1	..	..	..	..	..	..	..	6	6
2. Localised	..	..	18	12	18	8	9	6	7	7	3	3	2	..	..	..	..	..	57	36	93
IV. Tuberculous	60	23	69	77	19	37	13	21	2	4	4	2	1	..	..	..	..	..	168	164	332
V. Acute Infective	4	5	18	13	23	34	19	25	28	29	18	13	12	18	7	3	..	..	129	140	269
B. New growths—																					
I. Malignant	..	..	2	1	3	7	12	9	12	25	14	20	14	18	4	2	..	..	61	82	143
II. Benign	..	1	..	1	2	4	4	6	2	7	1	3	3	3	..	..	..	..	12	25	37
C. Abnormalities—																					
I. Floating Kidney	..	..	..	2	2	29	11	27	1	33	..	17	1	3	..	..	..	..	15	111	126
II. Various	..	1	1	..	..	2	..	2	1	1	2	..	..	..	..	..	..	..	4	6	10
D. Ascites	..	..	1	1	5	2	9	4	8	3	3	5	3	1	2	1	..	..	31	17	48
Totals	68	32	122	115	87	146	86	115	70	118	47	68	39	46	13	6	1	..	533	646	1179
	100		237		233		201		188		115		85		19		1		1179		
Percentages {Males	68		51·1		37·3		42·7		37·2		40·8		45·8		68·4		100		45·2		
at ages {Females	32		48·9		62·7		57·3		62·8		59·2		54·2		31·6		..		54·8		
Percentage to Total	8·48		20·11		19·76		17·05		15·49		9·75		7·22		1·61		0·08		100		

TABLE III.—*Tuberculous Peritonitis.*

	AGES.								TOTAL.
	1-9.	10-19.	20-29.	30-39.	40-49.	50-59.	60-69.	70+.	
Edinburgh Statistics .	65	129	49	30	6	6	1	...	286
Osler's Statistics . .	27	75	87	71	61	19	4	2	346
Total	92	204	136	101	67	25	5	2	632
Percentages . . .	14·55	32·25	21·50	15·99	10·60	4·0	0·8	0·31	...

A. LOCKHART GILLESPIE.